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ERRORS OF DIAGNOSIS IN PAEDIATRICS*

BY

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One of the few benefits which a physician gains from advancing years is experience through his mistakes. The account that follows is not only a personal confession, but also a review of some of the errors encountered during the course of thirty years in practice.

The subject requires some tabulating under various headings, which can be incorporated under four main aspects, all based on misconceptions or false interpretations. References are also made to overpopular diagnoses and to mistakes that are made by giving too much or, alternatively, too little significance to certain clinical features.

Disease Patterns in Adults and Childhood

Errors are sometimes made by imposing, as a kind of miniature replica, the pattern of disease of adults on to childhood. As a rule, in fact, illness in children tends to be much more acute and overwhelming, but there are some infections which have an entirely different clinical picture. Tuberculosis is a good example. Children with a chronic cough, mild pyrexia, anorexia, loss of weight, a debilitated look, and a history of sweating at nights are often thought to be tuberculous. Phthisis, which these symptoms suggest, does not occur in childhood, except in the rarest circumstances, and the diagnosis generally turns out to be an intestinal disorder once described by Eustace Smith as "mucous disease." Children with this disorder have a coated tongue, halitosis, and mucus in the stools. Sometimes threadworms are also present. Night sweats have probably raised the greatest suspicion, but this symptom is so common in childhood as almost to be physiological, if it is not the result of too much clothing and bedding, with lack of sufficient ventilation.

Otitis media in infants may progress without the usual warnings, and the drum finally ruptures after a stormy illness; earache may never have been present, or may have been difficult to establish. Vomiting and diarrhoea may have been the predominant feature, confusing the issue, and no reliance can be placed on pyrexia and leucocytosis, which may well be absent.

At this early age, also, quite advanced meningitis may occur before the right diagnosis is established. Rapid increase of intracranial pressure is largely avoided by separation of the sutures, so that the classical features of the disease do not arise until late, and various wrong conjectures are made. Bulging of the fontanelle instead of depression, to conform with the general state of dehydration and wasting, should finally throw true light on the condition.

Misconceptions

Perhaps the most dangerous diagnosis to make in an obviously sick infant is teething. Throughout the centuries it has been the refuge for doctors who are at a loss to know what is wrong. In this way I have known erysipelas, otitis, pyelitis, meningitis, and pneumonia go unrecognized. Although a physiological process, babies can be severely disturbed during the process, but all other sources of their trouble should be excluded before "teething" is blamed. The situation is not made any easier by the fact that during this episode the child's particular weakness may be set off, such as an attack of bronchitis or "croup," an intestinal upset, or even a fit.

Reactions of the blood to simple infections in children can be misinterpreted. Twice I have seen the lymphocytosis of pertussis labelled leukaemia. No diagnosis could be more serious, as the implications are so well known to most parents, and once made it is difficult to retract what has been said. With modern methods of bone-marrow puncture such a mistake could hardly occur.

Masked Clinical Picture

The course of pneumonia has been entirely altered by modern therapy, and it is rarely now a serious disease of some duration. Nevertheless, errors in its diagnosis and the oversight of other underlying conditions can occur. It can mask pertussis, which becomes obvious only as the pulmonary complication subsides. This may have troublesome consequences from spread of the infections to others in a ward before it is recognized.

In children, asthma is usually accompanied by so much catarrh and bronchial secretion that the clinical picture may be more like pneumonia. A history of repeated attacks of this nature of surprisingly short duration, and the association of an expiratory spasm with the general dyspnoea, should put the diagnosis straight and direct the correct treatment.

When an apparently straightforward case of pneumonia fails to react rapidly to penicillin or some other suitable antibiotic, and the clearing pulmonary skiagram reveals cyst-like cavities, the mystery of the protracted course seems to be explained. Still, it is unwise to jump to the conclusion immediately that cystic disease of the lung is present, as in some cases complete disappearance of the cavities eventually occurs. The "cysts" were

*Lecture delivered to the Plymouth Division of the British Medical Association on October 15, 1954.

abscesses which finally healed, and this can be demonstrated only by a series of *x*-ray films.

Turning to alimentary disorders, coeliac and fibrocystic disease (muco-viscidosis) in infants can be completely masked by diarrhoea. Gastro-enteritis which fails to improve with standard modern therapy after a reasonable period should raise a suspicion of one or other of these two disorders. Fibrocystic disease will be associated with very evil-smelling stools and possibly some pulmonary trouble as well.

One is never on safe ground in regard to appendicitis. To miss the condition in childhood is particularly serious, as peritonitis may so easily follow. An unusual position of the appendix behind the caecum or ascending colon is a well-known trap in the diagnosis, as then no tenderness and rigidity in the right iliac fossa need be present. I find that the good family doctor has an uncanny intuition in regard to this disease, and a specialist who disregards an opinion from that quarter is indeed a foolish man. When in doubt surely it is wiser to explore.

The situation has been further complicated by all too ready administration of antibiotics in doubtful cases. This can lead to an infected appendix being brought half under control; later it may rupture and produce a pelvic abscess. Diarrhoea may then be one of the main symptoms and, with the tense and tender abdomen, suggest some other abdominal disorder such as typhoid fever.

Misinterpreted Symptoms and Signs

Mothers often say they are able to tell the difference between their babies' crying from pain or from hunger; I wonder. The fact remains that the majority of infants who are brought to the doctor with supposed "colic" are suffering from underfeeding, and the trouble is easily remedied.

The aches and pains of muscular strain and spasm in genu valgum can be mistaken for those of subacute rheumatism, but rheumatic children seldom complain only of their legs. A much more serious error is to call osteomyelitis acute rheumatism. This has happened so often that a warning is given in most textbooks.

It should not be difficult to differentiate a tic from chorea, but they are continually being confused. When analysed, no choreic movement is entirely repetitive or can ever be said to have served a useful purpose. Children with tics, on the other hand, have insight into their ailment and can be encouraged to demonstrate their habit. The correct diagnosis is of more than academic importance, as the treatment of the two conditions is diametrically opposed.

A faint should be easy to distinguish from a fit if careful inquiry is made into the circumstances immediately preceding its occurrence, the aspect of the patient during the attack, and his behaviour afterwards. Emotional breath-holding in young children with resultant cerebral anoxia is easily recognized, although mistakes have been made and something more serious suspected. The real trouble arises in deciding whether a true fit is due to epilepsy or is merely an associated symptom of some febrile complaint. There are indeed some authorities who believe that "symptomatic" fits can occur only in potential epileptics. Certainly the E.E.G. gives some assistance, but one must always be quite convinced before labelling a child an epileptic.

Vomiting by its frequency in so many disorders of childhood inevitably leads to errors in diagnosis. Some newly born infants vomit all fluid for the first few days, and are soon thought to have a congenital abnormality of the alimentary tract. Abdominal distension and peristalsis are important signs in any form of intestinal obstruction, but are not always obvious and depend on the position of the lesion. Radiological evidence of pooling of air in the upper part of the gut and its absence at a lower level is sometimes helpful in the diagnosis, but fluid levels can be misleading. If meconium has been freely expelled and there is no bile in the vomit it is safe to wait. Passage of a rubber catheter into the stomach will exclude an oesophageal malformation. An unusual amount of mucus is often found in the vomit; this seems to be the main source of the trouble and can be remedied by gastric lavage.

Age is important. Certain diagnoses can be discounted on this alone—hypertrophic congenital pyloric stenosis, for instance, when symptoms first appear after the age of 3 months.

Vomiting and headache together are such classical features of serious intracranial disease that I hesitate to mention them. Errors are still made by the unwary, and the possibility of a brain tumour, tuberculous meningitis, or some other serious complaint must at least be considered. Migraine and cyclical vomiting should never be diagnosed until renal and cerebral disease have been excluded. With this in view the fundi are an important part of the physical examination. Lead-poisoning is rare, but should be noted as likely to give rise to a similar mistake.

There are a number of physical signs which are open to misinterpretation. An apical systolic murmur is commonly attributed to an organic lesion with little justification. It is a decision that must not be lightly taken; rheumatic carditis is usually diagnosed and the child unnecessarily condemned to a semi-invalid life. An intense murmur immediately after the first sound, with a fairly wide area of conduction, becoming louder on exercise and better heard with the child recumbent, is more likely to be due to an organic lesion. Cardiac enlargement, the presence of a thrill, and possibly a rheumatic history would be confirmatory evidence.

Paroxysmal tachycardia in infants may masquerade as an acute abdomen. Cardiac failure can rapidly appear, and the enlarged tender liver may give rise to such abdominal rigidity that it cannot be easily palpated. Vomiting may be present and the child show speedy signs of distress. Concentration on the abdomen may result in the tachycardia being overlooked. I have seen a case like this saved from surgical intervention just in time.

Another condition which may appear to be a surgical emergency is acute enterocolitis of the dysentery group with melaena, which has to be distinguished from intussusception. On the other hand, melaena is not necessarily present in all cases of intussusception, particularly when the condition is incomplete or recurring.

In the past, scurvy has also been mistaken for osteomyelitis.

It is perhaps not generally known that a transient glycosuria may occur after severe vomiting or starvation, with resulting ketosis. Further urinary tests should therefore be made, especially after the child has been given some sugar, before the possibility of diabetes mellitus is entertained. I need hardly remind you that coli bacilluria commonly gives rise to signs suggesting an acute abdominal condition, and that this urinary infection, acute appendicitis, tuberculous peritonitis, and enteric fever have all to be considered in a differential diagnosis. The physical signs of appendicitis and tuberculous peritonitis are sometimes so indistinguishable that laparotomy is the safest procedure.

Urethral valves in boys usually lead to bilateral hydronephrosis and hydroureters, which easily become infected. Sometimes congenital aplastic kidneys are present. Uraemia is the main feature, with vomiting and an intestinal upset. The enlarged ureters may be mistaken for dilated gut, and the whole clinical picture looks more like some alimentary disorder. As the condition is rare, this is all the more likely to happen.

A more common complaint is incontinence of faeces, and the child suffers from continuous soiling of his pants. Some of these cases find their way quite wrongly to child guidance clinics; others are diagnosed as Hirschsprung's disease. The rectum is found to be loaded right down to the anus, and

faeces can often be felt on abdominal palpation. The condition is really a very severe dyschezia due to bad bowel habits, sometimes originating from defaecation fears due to pain of an anal abrasion or fissure. Absence of enuresis should exclude any psychological factor.

On the other hand, a true case of Hirschsprung's disease may be overlooked in infancy when it presents all the features of lower intestinal obstruction. The most likely disorder with which it is apt to be confused in the immediate neonatal period is meconium ileus, the infantile variety of fibrocystic disease.

The only common blood disease which may lead the doctor astray is leukaemia, since it may first appear in various obscure ways—as a case of serious anaemia, agranulocytosis, purpura, generalized adenitis—or give rise to bone pains from subperiosteal deposits and be mistaken for rheumatism.

Only two neurological difficulties will be discussed. Todd's paralysis after an epileptic fit may persist for quite an appreciable time and cause anxiety in respect of some organic lesion of the central nervous system. "Otitic" or "toxic" hydrocephalus is a mysterious complaint which has quite often been confused with a brain tumour. No one could be blamed for subjecting a child to ventriculography and even more drastic measures when headache and vomiting with papilloedema are so striking. It is true there may be no localizing signs, but these are not invariably present with a centrally placed neoplasm. There seems to be no way of avoiding this mistake.

Finally, Still's disease may be puzzling when it arises with little or no arthritis, and merely with an irregular undulating fever, a rash, and a neutrophil leucocytosis. The possible diagnoses will then be legion. Alternatively, pericarditis may be present at the onset and rheumatic fever would then seem to be the correct diagnosis. It is perhaps not generally known that rheumatoid arthritis in childhood may first attack one joint alone. The fever, leucocytosis, and toxic state of the child will naturally lead to fear of a pyogenic arthritis, and the doctor in charge feels impelled to explore the joint for pus. The subject of Still's disease should not be left without referring to polyarteritis nodosa, which runs a very similar course.

Overpopular Diagnoses

Bronchiectasis is certainly diagnosed too readily. If there is a persistent productive cough, steps should always be taken to exclude a chronic sinus infection or segmental pulmonary collapse. Glandular fever is the other popular diagnosis which is consistently made on insufficient evidence. If adenitis is confined to the cervical region, tonsillar sepsis is a much more likely cause. Recently we have also been told that a glandular-like fever with eosinophilia but a negative Paul–Bunnell reaction may in fact be toxoplasmosis, an infection which is apparently commoner than we thought.

Finally, I would like to issue two warnings. One is against calling a child hysterical until all other possible causes have been excluded. Serious diseases can begin in this way. Meningitis, for instance, in children may produce most curious temperamental changes. Once I was very nearly misled in a case of subacute bacterial endocarditis. It arose in an excitable rheumatic girl of 12 years who was suddenly struck dumb on seeing her mother after an interval of three weeks. Apart from an old mitral lesion there was nothing else to discover. I was sorely tempted to consider the whole affair an hysterical outburst, but somehow refrained from this. There soon followed a right-sided hemiplegia which proved fatal, and the loss of speech was due to a small embolus in Broca's area.

It is easy to place too little significance on clinical features, but one can err in the opposite direction. Children have been confined to bed for months on end for a continued mild pyrexia—a "ninety-niner" it could be called—with no symptoms, no signs, no leucocytosis, a normal sedimentation rate, and all investigations negative. Surely the advice here is to throw the thermometer out of the window and allow the child to get up.

So ends what I have to say. My remarks have probably been of little value. Growing children rarely profit by the mistakes of others; they have to make their own experiences. I wonder if adults are any better, even those who belong to our profession.

Congreve was indeed wise when he wrote, "Error lives ere reason can be born."

A "FOLLOW-UP" CHEST X-RAY SURVEY IN THE RHONDDA FACH

I. PULMONARY TUBERCULOSIS

BY

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Consultant in Chest Diseases, Pontypridd and Rhondda District

AND

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Techniques for evaluating the effect of various therapies on groups of individuals have recently been much studied and most effectively applied both in the tuberculosis and in other fields. This report attempts the more difficult task of evaluating the effect of preventive medicine on a community.

In 1950–1, as the first step in a long-term investigation of the aetiology of progressive massive fibrosis (the more serious form of coal-workers' pneumoconiosis), 89.0% of the inhabitants of the Rhondda Fach over the age of 15 were *x*-rayed (Cochrane *et al.*, 1952). In addition, owing to the ready co-operation of the Welsh Regional Hospital Board, we were able to offer immediate admission to hospital to all "active" cases. In this way the inhabitants of the valley may be said to have received "radical" therapy for tuberculosis.

It will be argued by some that the technique would have been more radical if B.C.G. had been given to all those whom we found to be tuberculin-negative at the time of the first survey. This was not done for two reasons: (1) we did not think the evidence in favour of B.C.G. so convincing that it would be unethical not to vaccinate the tuberculin-negative, and (2) we were particularly anxious to measure the "conversion" and "reversion" rates. Tuberculin-negative children under 5 years of age were, however, given B.C.G. if they were "contacts," while older "contacts" were similarly vaccinated if their parents so wished.

In 1953, during the second stage of the investigation, the community was again *x*-rayed, and we are therefore in a position to measure the changes in the death rate and prevalence rate of tuberculosis and measure the attack rate of infection.

It is, however, impossible to cover all this in detail in one report. The epidemiology of pneumoconiosis,

including a discussion of the relationship between tuberculosis and progressive massive fibrosis—the main object of the scheme—has in general been reserved for a separate publication, and further papers will deal with such subjects as the results of tuberculin-testing and the factors influencing the attack rate of tuberculosis.

General Description and Plan of Work

(1) First Survey

We were conscious that there were some errors inherent in the techniques used at the time of the first survey, so advantage was taken of the second survey to reduce them. Fortunately, however, the errors discovered were small, but they necessitated some slight modifications of the results we published in 1952. In this report, the tables and diagrams incorporate these corrections.

(2) Between the Surveys

All those who were thought to be suffering from active tuberculosis were hospitalized, with two exceptions, at the time of the first survey. As expected, it was not found possible to keep all the infectious cases in hospital. After the first few months there were nearly always 40 known infectious cases in the valley, between the two surveys, who were carefully supervised by the health visitor.

Figs. 1 and 2 show the death rates from pulmonary tuberculosis amongst the men and women in the valley between 1949 and 1953. In Fig. 2 the female death rates are compared with those for the rest of the Rhondda Urban District (population 111,389), which is also predominantly a mining area.

The rates for women show (*a*) that the tuberculosis mortality in the Rhondda Fach was originally higher than in the rest of the R.U.D.; (*b*) that at the time of the first survey there was a slight rise (this was possibly due to more accurate notification of cause of death); and (*c*) that after the survey the death rate fell rapidly and was actually zero in 1953. The figures are small (Table I), but encouraging so far as they go. The rates for non-miners are very similar.

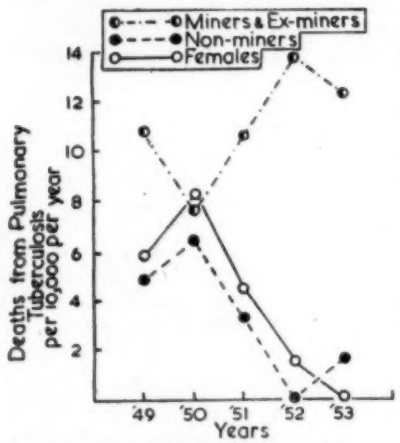

FIG. 1.—Crude tuberculosis death rates in the Rhondda Fach.

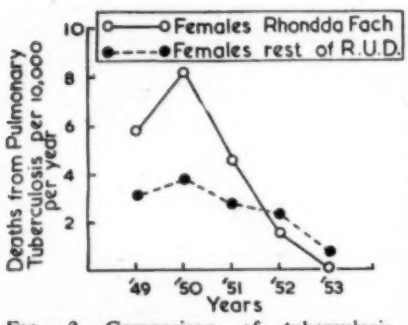

FIG. 2.—Comparison of tuberculosis death rates among females in the Rhondda Fach with those in the rest of the Rhondda Urban District.

The figures for miners and ex-miners are possibly less depressing than they appear. Shortly after the survey started, another research project led to an ever-increasing proportion of miners and ex-miners in this area upon whom a post-mortem examination had been made. In 1953, more than 50% of such men who died had a post-mortem examination. This is very satisfactory from one point of view, but the increasing appearance of tuberculosis in the death certificates is almost certainly related to the increasing proportion of necropsies. It must be remembered that only 1% of cases of progressive massive fibrosis (P.M.F.) give a positive sputum in life (Cochrane *et al.*, 1952), while nearly 40% are positive bacteriologically at necropsy (James, 1954). It is not surprising, therefore, that the rates for miners and ex-miners have not shown the same fall as those for the females. However, it seems clear that mortality from tuberculosis among miners and ex-miners will remain a serious problem in South Wales long after it has virtually disappeared amongst the others.

TABLE I.—*Deaths from Pulmonary Tuberculosis in the Rhondda Fach, 1949–53*

	Estimated Population	1949		1950		1951		1952		1953	
		No.	‰	No.	‰	No.	‰	No.	‰	No.	‰
Females ..	13,464	8	5·9	11	8·2	6	4·5	2	1·5	0	0·0
Miners and ex-miners	6,513	7	10·7	5	7·7	7	10·7	9	13·8	8	12·3
Non-miners	6,207	3	4·8	4	6·4	2	3·2	0	0·0	1	1·6

(3) Second Survey

This second survey had three main objectives: (1) to reinforce the effect of the first survey in controlling tuberculous infection in the area; (2) to evaluate the effect of the first survey; and (3) to reduce the errors inherent in some of the techniques used in the first survey.

(4) General Method of Work

Our general approach was very similar to that used during the first survey, but the following changes were introduced: (*a*) We were, on this occasion, interested in two overlapping populations, the defined 1950–1 population (Population A), of which a nominal roll was made, and the 1953 population (Population B), which was defined by private census just before the survey started. This was found preferable to our previous use of corrected electoral rolls. (*b*) A records card (Fig. 3) was completed for everyone in the valley, in addition to the M.M.R. cards and P.R.U. industrial histories. They were also used for checking against the two populations, and were later coded and used as a basis for a punch-card analysis.

One point in connexion with the analysis must be stressed. The year of birth was punched in each case, but, as the time interval between the two surveys was 2 years 7 months (2.6 years), it was impossible to carry out an analysis by age at the time of each survey without either overestimating or underestimating the age at the time of the second survey in relation to that at the first survey. We have chosen, in effect, to overestimate the age (by 0.4 years) at the time of the second survey, and allowance for this must be made when interpreting some of the figures and tables.

Details of our methods of work are given in the Appendix.

Results

(1) The Defined Population

The two populations were in general defined as consisting of those of 5 years of age and over who were living in each town at the end of the survey there.

Some points, however, require greater definition. The survey did not take place at a single point in time; it lasted several months. It was therefore decided to consider the population as a composite one. The population of each town was defined as those inhabitants who were alive at the end of the survey in that particular town. The concept "inhabitant" also needed clearer definition. We were chiefly interested in these populations from the point of view of infection, so the time spent at home was the most important factor. We therefore excluded those who were in the armed Forces or who were "working away" unless they came home regularly at week-ends.

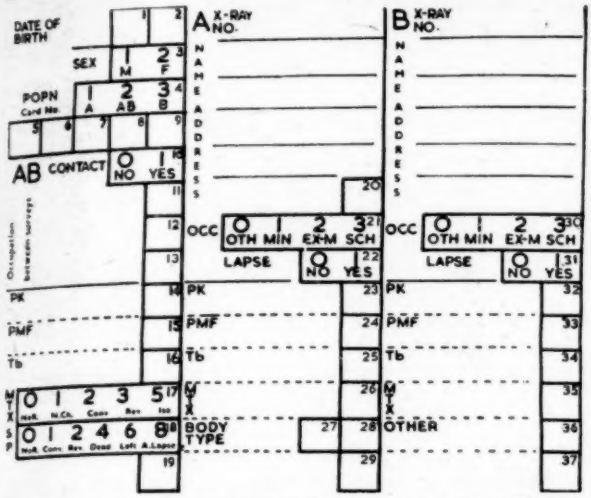

FIG. 3.—The records card designed for use in the follow-up survey.

The Population B is analysed in Fig. 4. In Table II Population A is compared with Population B and also with our previous estimate. The differences between the two estimates of Population A are small (59 in the case of men and 31 in the case of women).

Lewis-Faning (1953) compared the age distribution of our survey population with that of Wales as indicated by the preliminary figures of the 1951 Census, and suggested that either the population of the Rhondda Fach diverged markedly from that of Wales as a whole, or we had not completely enumerated its population.

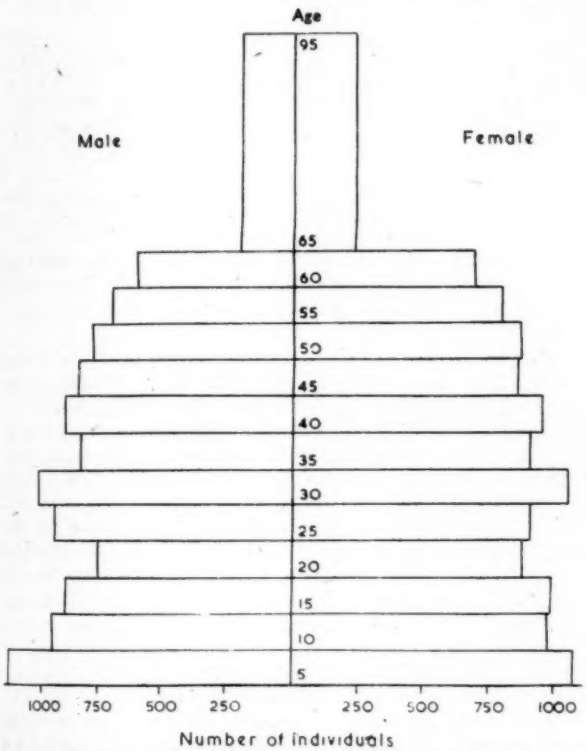

FIG. 4.—Rhondda Fach. Defined population at time of 1953 survey.

However, on re-checking our population we were not able to discover any source of error, and, indeed, subsequent publication of the 1951 Census County Report of Glamorgan (Registrar-General, 1954) showed the age distribution of the Rhondda Urban District (of which the Rhondda Fach is a part) to be very similar to that which we published.

(2) Population X-rayed

The same criteria were used as in the previous survey—that is, the population *x*-rayed consisted of those who were over the age of 5 at the time of the survey, and of whom a technically acceptable radiograph had been obtained by one of the teams or by anyone else within six months of the survey, provided the film was either made available to us or had been read by some recognized authority. The remainder of the population were termed "lapses." All films were read in duplicate and sputum investigations were carried out on a large scale. The 35-mm. films were read independently by two observers (T. F. J. and Dr. W. E. Miall) and the 14 by 14-in. (35 by 35-cm.) films by two pairs of observers (A. L. C. and Dr. Idris Davies, and Drs. P. J. Chapman and S. Rae).

Tables II and III summarize the percentage *x*-rayed in the two surveys. The differences are chiefly in the younger age groups, and are probably due to the better definition of the population on the second occasion. All prevalence rates refer to these *x*-rayed populations.

TABLE II.—*Defined and X-rayed Populations* 1950–1 *and* 1953

Age	Population 1950–1 as Measured Then			Population 1950–1 Corrected 1953			Population, 1953		
	%	No. X-rayed	No. in Population	No. in Population	No. X-rayed	%	No. in Population	No. X-rayed	%
				Females					
5				1,000	929	92·9	1,072	1,054	98·3
10				1,005	942	93·7	977	960	98·3
15	(95·6)	(758)	(793)	972	903	92·9	990	964	97·4
20	93·0	787	847	887	807	91·0	867	824	95·0
25	94·1	994	1,056	1,041	970	93·2	906	866	95·6
30	92·5	889	961	977	903	92·4	1,047	985	94·1
35	92·2	913	990	982	903	92·0	904	833	92·1
40	91·0	810	890	896	817	91·2	952	856	89·9
45	88·5	785	888	898	779	86·7	852	767	90·0
50	87·5	770	880	885	775	87·6	867	761	87·8
55	86·8	645	743	743	631	84·9	787	684	86·9
60	78·6	503	640	654	509	77·8	690	567	82·2
65	59·2	751	1,269	1,260	750	59·5	1,430	968	67·7
Total	86·4	8,605	9,957	12,200	10,618	87·0	12,341	11,089	89·9
Total (20+)	85·6	7,847	9,164	9,223	7,844	85·0			
				9,164	7,847				
			Error	59	3				
				Males					
5				975	898	92·1	1,165	1,145	98·3
10				1,010	955	94·6	953	935	98·1
15	95·4	721	756	891	826	92·7	892	870	97·5
20	95·4	760	798	819	768	93·9	748	703	94·0
25	94·0	958	1,019	1,020	958	93·9	940	889	94·6
30	92·9	804	865	870	805	92·4	1,017	958	94·2
35	94·4	828	877	892	840	94·2	829	776	93·6
40	93·2	840	901	906	838	92·5	896	831	92·7
45	93·7	760	811	809	751	92·8	841	776	92·3
50	93·2	700	751	748	704	94·1	771	702	91·1
55	93·2	647	694	684	629	92·0	699	623	89·1
60	90·7	558	615	642	576	89·7	602	539	89·5
65	78·0	916	1,174	1,146	902	78·7	1,195	986	82·5
Total	91·7	8,492	9,261	11,412	10,450	91·6	11,548	10,733	92·9
Total (20+)	91·4	7,771	8,505	8,536	7,771	91·0			
				8,505	7,771				
			Error	31	—				

The total age 20 and over was chosen for comparison between the two 1950–1 populations as the 15–19 age group excluded those still at school on the first occasion.

TABLE III.—*Summary of Percentages X-rayed in the Two Surveys Over the Age of* 5

	Population 1950–1 Corrected 1953			Population 1953		
	No.	No. X-rayed	%	No.	No. X-rayed	%
Males	11,412	10,450	91·6	11,548	10,733	92·9
Females	12,200	10,618	87·0	12,341	11,089	89·9
Total ..	23,612	21,068	89·2	23,889	21,822	91·3

TABLE IV.—*Females. Prevalence of Tuberculosis in the Rhondda Fach, 1950–1 and 1953*

Age	Survey 1950–1							Survey 1953						
	Pop. *X*-rayed	No. Infectious	°/₀₀	No. Active Including Infectious	°/₀₀	Quiescent and Active	°/₀₀	Pop. *X*-rayed	No. Infectious	°/₀₀	No. Active Including Infectious	°/₀₀	Quiescent and Active	°/₀₀
5	929	—		6	6·5	6	6·5	1,054	—		—		7	6·6
10	942	3	3·2	10	10·6	10	10·6	960	4	4·2	4	4·2	10	10·4
15	903	5	5·5	13	14·4	16	17·7	964	4	4·1	7	7·3	18	18·7
20	807	19	23·5	30	37·2	45	55·8	824	1	1·2	14	17·0	36	43·7
25	970	10	10·3	13	13·4	22	22·7	866	5	5·8	18	20·8	41	47·3
30	903	14	15·5	18	19·9	23	25·5	985	7	7·1	12	12·2	17	17·3
35	903	5	5·5	9	10·0	12	13·3	833	5	6·0	8	9·6	15	18·0
40	817	1	1·2	2	2·4	5	6·1	856	1	1·2	4	4·7	11	12·9
45	779	4	5·1	5	6·4	5	6·4	767	—	—	—	—	3	3·9
50	775	—	—	—	—	—	—	761	3	3·9	4	5·3	5	6·6
55	631	—	—	—	—	1	1·6	684	2	2·9	2	2·9	2	2·9
60	509	—	—	—	—	1	2·0	567	1	1·8	3	5·3	3	5·3
65	750	3	4·0	3	4·0	4	5·3	968	1	1·0	1	1·0	2	2·1
Total	10,618	64	6·0	109	10·3	150	14·1	11,089	34	3·1	77	6·9	170	15·3

Fig. 5 shows the percentage of miners, ex-miners, non-miners, and women who were *x*-rayed during the second survey. Although age appears to be the most important factor influencing the lapse rate, occupation and sex also appear to be important.

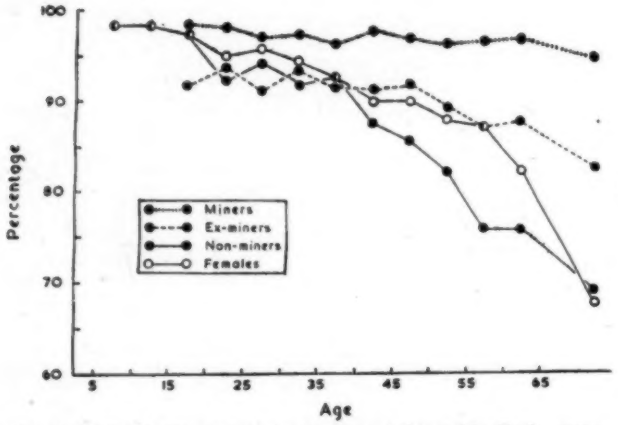

FIG. 5.—Percentage *x*-rayed in the second Rhondda Fach survey.

(3) Prevalence of Tuberculosis

(a) Prevalence of Tuberculous Infection.

The schoolchildren were again "Mantoux"-tested by one of us (T. F. J.), and Fig. 6 summarizes the results. The change appears satisfactory, but the results will be discussed in greater detail in a subsequent paper.

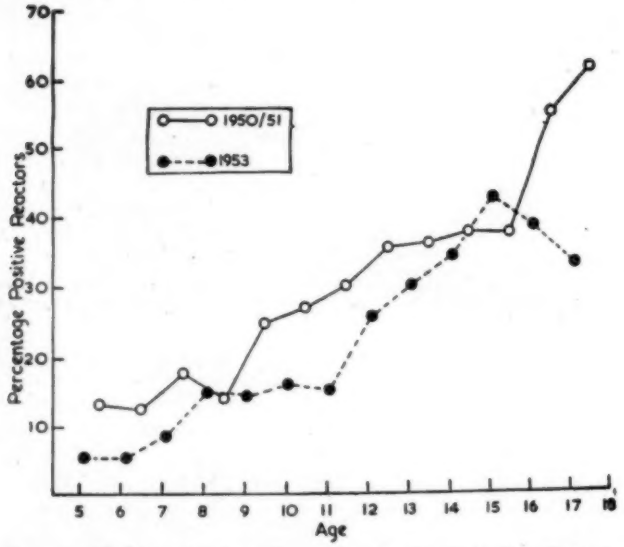

FIG. 6.—Results of tuberculin testing in the Rhondda Fach in 1950–1 and 1953. (In this figure the ages have been adjusted to correct for the error of 0.4 year.)

(b) Prevalence of Tuberculous Disease

The same standards of diagnosis were made as on the previous occasion. Fig. 7 and Table IV show the prevalence of infectious tuberculosis amongst the women at the time of the two surveys. It is clear that there has been a satisfactory fall. So far as miners are concerned, however, a similar decrease is seen only amongst the younger miners

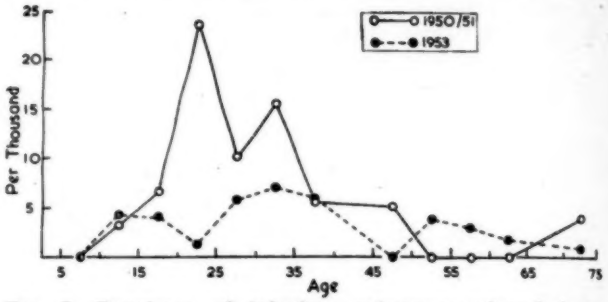

FIG. 7.—Prevalence of infectious pulmonary tuberculosis in Rhondda Fach females.

and ex-miners (Fig. 8); in the higher age groups there has been a definite increase. The results for the non-miners are somewhat difficult to interpret owing to their atypical age distribution (Fig. 9).

Those who had a positive sputum at the time of the first survey have been analysed in terms of their status at the time of the second survey (Table V). This assists us to understand some of the changes that have taken place in the prevalence of pulmonary tuberculosis. The lower mortality rate among females as shown in Fig. 1 would, of course, tend to increase rather than decrease the prevalence of infectious pulmonary tuberculosis. The cause of the fall must therefore be looked for elsewhere. The females have the highest rate of conversion from "positive" to negative sputum, and this may very well be an important factor contributing to the fall in prevalence. The highest sputum conversion rate is found among females in the younger age groups, and the lowest among cases of P.M.F., which corresponds with general clinical experience in the area. Although these overall conversion rates are relatively high, the number of cases that remained positive after treatment certainly suggests that there is still room for great clinical advances. Amongst the males with positive sputum at the time of the first survey there were 12 cases of P.M.F. It is of great interest that only one of them died during the

TABLE V.—*Status in 1953 of the Infectious Cases at the Time of the 1950–1 Survey*

	No. of Infectious Cases 1950–1	Status of the Same Cases in 1953						No. who Left the Area
		No. Dead	%	No. Sputum Negative	%	No. Still Sputum Positive	%	
Males ..	48	7	14·6	19	39·6	20	41·7	2
Females ..	64	7	10·9	41	64·1	15	23·4	1

2.6 years between the surveys. This is very different from that found by Kilpatrick *et al.* (1954), who reported that 80% of such patients were dead in 2½ years. The difference may be partly due to the cases seen by Kilpatrick being

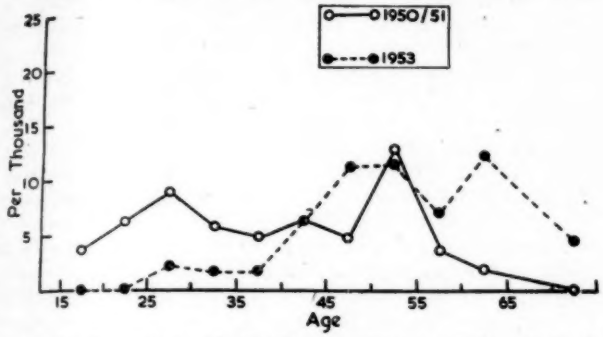

FIG. 8.—Prevalence of infectious pulmonary tuberculosis in Rhondda Fach miners and ex-miners.

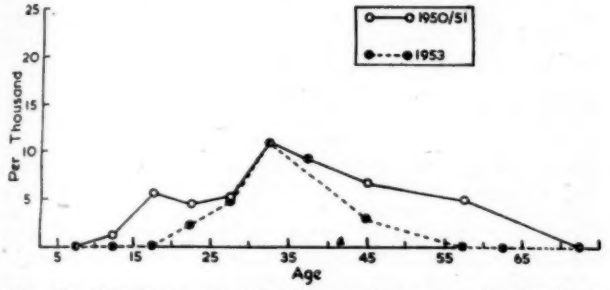

FIG. 9.—Prevalence of infectious pulmonary tuberculosis in Rhondda Fach non-mining males (owing to small numbers in higher age groups these have been combined to give a smoother curve).

selected on the basis of severity or, more probably, to the effect of antibiotics which have been used in the treatment of our cases, and which appear to prolong life without, unfortunately, causing sputum conversion.

No marked changes could be expected in the total prevalence of all types of tuberculosis, as the main way of leaving the tuberculous population is the extremely slow one of progression from the group with "active" tuberculosis to that with "quiescent" disease, and finally to the group which has "arrested" disease. The small change in total prevalence that has occurred amongst females is shown in Fig. 10. It should, however, be stressed that, although the reduction in total prevalence of all types of pulmonary tuberculosis is small, the qualitative changes within this "tuberculous" population represent a very real improvement in the tuberculosis situation in the valley. A very important factor in causing changes in prevalence is, of course, the "attack rate" of new cases, which is considered below.

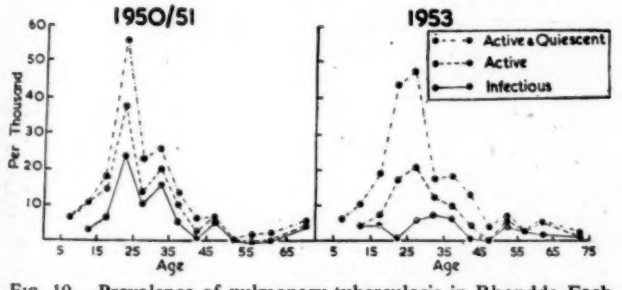

FIG. 10.—Prevalence of pulmonary tuberculosis in Rhondda Fach females.

(4) Attack Rate of Pulmonary Tuberculosis

This index measures the rate of appearance of shadows considered clinically to be tuberculous amongst those whose *x*-ray films were previously considered to be free of tuberculosis. Cases of definite simple pneumoconiosis (Categories 2 and 3) which developed early signs of progressive massive fibrosis are not included in this paper. They will be dealt with in a subsequent paper. The accuracy of such measurements depends mainly on the extent to which the original population has been followed up, and our results in this respect can conveniently be considered here.

Those who were *x*-rayed during the first survey fell into three groups at the time of the second survey: (1) those who had died in the interval, (2) those who had left the defined area, and (3) the survivors. The last-named could be further subdivided into those *x*-rayed again at the time of the second survey and those who refused.

The extent of the follow-up is shown in Table VI. It will be seen that 95% of the "surviving" men and women were *x*-rayed. This is shown diagrammatically in Fig. 11 for the women.

In order to calculate the attack rate on those whose *x*-ray films were considered normal as regards tuberculosis at the time of the first survey, those with active and quiescent

TABLE VI.—*Summary Results of the "Follow-up" of Those X-rayed in* 1950–1

	X-rayed 1950–1 (1)	No. Dead (2)	% of (1)	No. Left Area (3)	% of (1)	No. Remaining (4)	% of (1)	No. Re-*X*-rayed (5)	% of (4)
Females ..	10,618	168	1·6	650	6·1	9,800	92·3	9,315	95·1
Non-mining males ..	4,310	47	1·1	515	11·9	3,748	87·0	3,612	96·4
Miners and ex-miners	6,140	308	5·0	330	5·4	5,502	89·6	5,200	94·5
Total ..	21,068	523	2·5	1,495	7·1	19,050	90·4	18,127	95·2

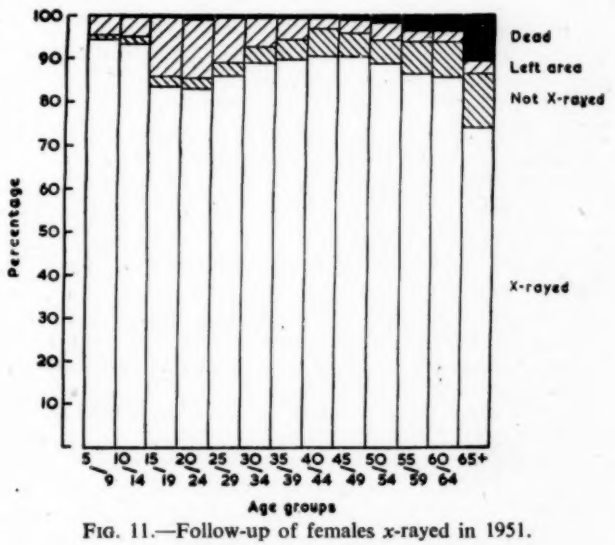

FIG. 11.—Follow-up of females *x*-rayed in 1951.

lesions were excluded from the population of those *x*-rayed in 1950–1. When pulmonary tuberculosis was diagnosed during the second survey on 35-mm. film, and the records showed that the person concerned had been *x*-rayed and the *x*-ray considered normal on the previous survey, the two films were projected simultaneously and scrutinized by three readers. The technique was time-consuming but very satisfactory.

Fig. 12 shows the radiological attack rate of tuberculosis amongst women, non-miners, and miners and ex-miners whose films were read as "normal" for pneumoconiosis and tuberculosis at the first survey.

It is proposed to devote a later paper to a discussion of the attack rate of tuberculosis and the factors influencing it. We can, however, make the following points conveniently at this stage.

(1) We have clearly not succeeded in preventing the appearance of new tuberculous lesions, and owing to the

absence of any previous direct measurement of the attack rate in that area we cannot claim to have reduced it.

(2) Our figures in general confirm the pioneer measurements of attack rate made by Springett (1951), which are still the only ones available, as shown in Table VII. Superficially, too, it would appear that our attack rates are very similar to his in magnitude, suggesting that the first survey had little or no effect on the attack rate. It must, however, be remembered that Springett's data are not entirely comparable with ours. His measurements inevitably excluded those who, after a normal film, developed symptoms later and were diagnosed at clinics or hospitals (Springett, 1951), which would lead, as he points out, to his attack rates being underestimates. In addition, Springett (personal communication, 1954) did not include in his series cases of uncomplicated primary type tuberculosis or pleurisy. This again would make his figures a considerable underestimate in relation to ours, which include both types. In Table VII a crude attempt has been made to allow for these differences by excluding from our series (*a*) cases of uncomplicated primary type tuberculosis and pleurisy, and (*b*) those who went to the clinic between the surveys on account of symptoms. Such an approach, it must be stressed, is very crude, as the factors influencing people to go to the clinic in the Rhondda Fach after the first survey were probably very different from those influencing Civil Servants in London. The comparison does, however, suggest that the attack rate in the Rhondda Fach between the surveys was less than that of Civil Servants in London in 1946–9.

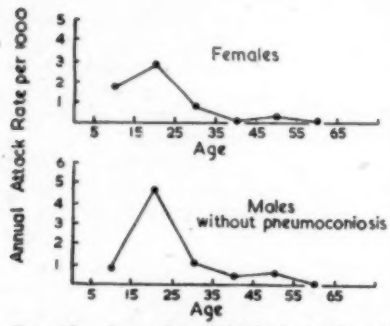

FIG. 12.—Annual radiological attack rate of tuberculosis in the Rhondda Fach.

TABLE VII.—*Annual Radiological Attack Rates of Tuberculosis per Thousand*

Source of Data	Females		Males without Pneumoconiosis	
	Age 15–24	Age 25–34	Age 15–24	Age 25–34
Rhondda Fach surveys 1950–1 and 1953	2·8	0·7	4·7	1·0
Springett (1951). London	3·5	2·0	3·0	2·0
The same Rhondda Fach data but excluding uncomplicated primary type tuberculosis, pleurisy, and those who were diagnosed between surveys on account of symptoms	0·6	0·7	0·4	1·0

(3) The way in which the appearance of new cases is confined to the younger age groups suggests the possibility of selective follow-up when a community has already been carefully surveyed. In a community where there is no progressive massive fibrosis it would be very reasonable to restrict the follow-up to those under the age of 35. The one female "new" case over this age was a diabetic. It would, of course, be necessary to have a careful follow-up of all male minimal quiescent lesions as well.

Discussion

From the point of view of epidemiology in general, our most important finding is a purely technical one. We have shown that it is technically possible to follow up a population of 25,000 people with a relatively low lapse rate. We believe this to be of considerable importance in the field of experimental preventive medicine.

As regards the epidemiology of tuberculosis, the most important finding is the confirmation of Springett's work that the radiological attack rate of tuberculosis in the two sexes has a very similar age distribution in spite of the marked differences between the sexes in the relationship of tuberculosis mortality to age. This suggests, as Springett pointed out, that the higher tuberculosis mortality now being experienced by males in the higher age groups is mainly caused by the breakdown of lesions acquired in early adult life.

From the point of view of practical tuberculosis control, our results are less striking than we had hoped but less depressing than we had feared. There was a marked fall in tuberculosis mortality amongst women and non-miners; there was a considerable reduction in the prevalence of infectious cases, particularly among the younger people, and there was probably a reduction in the attack rate of tuberculosis.

The effects of such community surveys have recently been reviewed (Cochrane, 1954). There is no other survey with which a detailed comparison can be made. Olsen (1953) showed that the mortality rate was halved but that there was relatively little change in the notification rate after an extensive survey in Bornholm. The greater fall in mortality achieved in the Rhondda Fach is probably due to the availability of antibiotics after the first survey (the first Bornholm survey was completed in 1940). No details are given of changes in attack rate or prevalence rate, so no further comparison is possible with Bornholm. It is, however, of interest that there is nothing to suggest that a greater effect was achieved in Bornholm, where B.C.G. was given on a large scale in addition to hospital treatment. Davies (1946) and Davies *et al.* (1948) reported very much more striking results. In one instance no new cases were found during six years after *x*-raying a community of 367 and only one new case in the three years following a community survey of 6,000 people. The differences between their results and ours are possibly due to a very much lower initial prevalence in the communities they *x*-rayed, but unfortunately there is little evidence available on this point.

There are some points in relation to the results which deserve more detailed discussion:

(1) Of the 112 infectious cases known to us at the time of the first survey, all but two had had treatment and many had had surgical treatment. In 1953 14 were dead and 35 were still sputum-positive. This is a rude reminder that the therapeutic battle is only half won.

(2) If, as now seems probable, the tuberculous lesion in the male has a relatively long period of latency before cavitating and becoming infectious, the problem, as Springett pointed out, is a serious one, as the numbers are large and the period of observation long. Progressive massive fibrosis, probably pathologically and certainly administratively, presents this problem in its most serious form. These lesions are very slowly progressive over long periods of time, but may at any time become very infectious. Chemotherapy has undoubtedly improved their prognosis *qua vita*, but sputum conversion is only rarely achieved, and is even more rarely permanent. This group is undoubtedly the most serious obstacle to the elimination of tuberculosis from the valley.

(3) The speed at which the tuberculosis mortality rate fell in the valley, while the overall prevalence was scarcely altered, indicates that the mortality rate by itself is not an adequate index of prevalence. In addition, as mortality approaches zero it becomes less and less sensitive as an epidemiological index. This underlines the need for a new index. It is improbable that notification rates, however complete they are made by "intimation" or other means, and however much the inter- and intra-observer error is reduced among chest physicians, will ever be really satisfactory. In the discussion of new indices, too little attention has been paid to deciding which epidemiological index one wishes to estimate. If mortality indices are unsatisfactory, the only alternatives are attack rates, and no one would suggest it as a satisfactory routine measure.

Prevalence rates are not such a valuable measurement from the point of view of preventive medicine as attack rates, because changes in them are often rather difficult to interpret, since they vary directly with the attack rate and

inversely with the case fatality rate; but when the case fatality rate is low—as it soon will be in tuberculosis—they are much more satisfactory. They will, in any case, measure the administrative and social load on the community. Prevalence, unlike the attack rate, can, theoretically, be measured relatively accurately by *x*-raying a random sample of the community, and the way is thus open for obtaining a satisfactory index for various parts of the country. Whether this is a practical possibility can, of course, be decided only by actual experience.

(4) The relation between the effort put into the Rhondda Fach surveys and the results obtained should give other workers some idea of the effort required to eliminate tuberculosis from the country.

Summary

Part of the second stage of a field experiment in the Rhondda Fach to investigate the effect of reducing tuberculous infectivity upon the rate of appearance of progressive massive fibrosis in miners is described.

The valley was re-surveyed in the summer of 1953. On this occasion we succeeded in *x*-raying 91.3% of the new population over the age of 5, and 95% of those who had been previously *x*-rayed and who were still resident in the valley. The prevalence of infectious tuberculosis as compared with the figures at the time of the first survey (1950–1) shows a marked fall amongst the women and a lesser fall amongst the younger men. There has been a slight increase amongst the older miners and ex-miners.

The tuberculosis mortality for women and non-miners has fallen sharply between the two surveys. The same trend is not shown for miners and ex-miners.

In spite of ample hospital accommodation, 35 (amongst whom were 10 cases of progressive massive fibrosis) of the 112 cases which were infectious in 1951 were still infectious in 1953, and 46 new cases of tuberculosis developed in the valley between the two surveys.

APPENDIX

A. General Method of Work

As a result of our previous experience, we relied mainly on home-visiting as a means of persuading people to be *x*-rayed. Only one broadcast appeal was made, and there was little publicity in the Press. The actual *x*-raying was done between April 7 and July 31, 1953. In spite of the holidays which inevitably interfered with the survey, this was found preferable to the previous winter survey.

The staff was considerably enlarged in comparison with the previous survey. The Welsh Regional Hospital Board supplied two M.M.R. teams for most of the duration of the survey, and the Medical Research Council's P.R.U. team was assisted by two teams who were being trained for work with the National Coal Board. The *x*-raying was done at five main centres in the valley, at each of which there were (1) a mobile 35-mm. unit, *x*-raying the schoolchildren; (2) a "fixed" 35-mm. and a "fixed" 14 by 14 in. (35 by 35 cm.) unit in the centre of the town, *x*-raying women, non-miners, and ex-miners; and (3) a mobile 14 by 14 in. unit at the pithead *x*-raying miners. Slight modifications were introduced at each centre to suit local conditions. At the main centre, *x*-raying was continuous from 10 a.m. until 10 p.m., for women, children, ex-miners, and non-miners. On several occasions the mobile *x*-ray van (35-mm. film) was taken into the streets, but the results were less spectacular than expected.

We were, on this occasion, interested in two overlapping populations: (1) the "defined" population, of 1950–1 (Population A), and (2) the new population of those living in the same geographical area in 1953 (Population B). For Population A, a typewritten nominal list was prepared from our previous records in street number order, including name, initials, address, and previous *x*-ray number for those *x*-rayed in the first survey. Population B was obtained by a private census which antedated the survey by about two weeks. The technique proved highly satisfactory—much superior to our previous technique with electoral rolls.

A card was designed (Fig. 3) giving details of both surveys. These cards were completed at the three centres for everyone *x*-rayed, in addition to the usual M.M.R. cards and P.R.U. industrial histories. These cards were then sent from all four *x*-raying units to a central bureau, where they were sorted by streets and then checked first against Population B and then against Population A lists. Owing to the details available about each person, a very accurate check was possible. In the case of any doubt the person was visited. This served as a check on the accuracy of both Populations A and B. Those not marked as *x*-rayed on Population B were visited and, when possible, persuaded to be *x*-rayed. This proved a very much more difficult task than on the previous survey. This was possibly due to the lack of propaganda, but that was not our impression. Subsequently, Population A was checked against Population B, and the addresses of all those not marked as *x*-rayed or as refusals on the second survey were visited to discover whether the person was dead, had left the area, or whether there had been a mistake on one or other of the populations. Later, Population B was checked against Population A to discover, in the case of those members of Population B not *x*-rayed during the second survey, whether they were in Population A, and, if not, where they were living at the time of the previous survey. All this involved a great deal of home-visiting, but led to a great increase in accuracy in the definition of both populations.

The punching of the material on Hollerith cards and the subsequent analysis were carried out under the supervision of Mr. R. G. Carpenter, of the Pneumoconiosis Research Unit.

B. Radiographic Technique

The P.R.U. work was done under the supervision of Mr. W. G. Clarke. The P.R.U. mobile van was re-equipped with a Siemens four-valve unit with an output of 125 kV and 500 mA. The tube-cassette stand was specially designed for use in a van and ensured that the tube was always correctly centred to the film. Exposures were controlled by the "iontomat," the new automatic exposure control which incorporates an ionization chamber to measure the *x*-radiation reaching the film. The processing of the films in the van was done using the N.R.D. automatic processing unit. Electrical power was supplied by a mobile diesel generator of large capacity, 32 kVA. This also supplied power for the heating of the tents and a second mobile van which was used for film reading. This unit operated at the pithead.

A second unit, a Victor KX8, which had been installed in the van for the first survey, was assembled in the various halls and chapels and was used for the examination of ex-miners. Large film retakes, requested by the M.M.R. unit, were also taken on this unit. Power was supplied for this unit by a generator with the same output as that supplying the van.

M.M.R. units were installed in the same halls and staffed by the mass radiography service of the Welsh Regional Hospital Board, under the administrative direction of Mr. John H. Phillips. These units were responsible for the examination of women, children, and non-miners. The M.M.R. technique was exactly similar to that described for the first survey.

The proximity of the two units introduced the possibility of excessive scatter radiation affecting the staff. This was overcome by the use of lead screens. That this was effective was shown by checks made on dental film worn by the staff and measured by the N.P.L.

Acknowledgments.—The difficulties of making adequate acknowledgment in work which involves the active assistance of so many people increase as time passes and the personnel changes. But we wish to record our gratitude to the many members of the staff of the Welsh Regional Hospital Board and their Mass Radiography Service. the Pneumoconiosis Research Unit, the Public Health Laboratory Service, Tyntyla Hospital, Pontypridd

Chest Clinic, the National Coal Board, and the National Union of Mineworkers; and especially to the members of the two teams who gave such devoted service, and to the men, women, and children of the Rhondda Fach, without whose co-operation the scheme would have been impossible.

We express our thanks for the assistance given by the members of the Local Advisory Committee of the Rhondda Fach Scheme, and in particular to the members of its executive subcommittee. The views expressed in the paper are, however, our own and not necessarily those of the members of the Committee.

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AORTIC ANEURYSM DUE TO TUBERCULOUS LYMPHADENITIS

BY

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The term "mycotic aneurysm" was first used by Osler in 1885 when he described a patient with multiple aneurysms of the aorta secondary to what he termed "malignant mycotic endocarditis." Since then a group of diseases have been named the mycoses, and so the word "mycotic" has been given another meaning in addition to its original one. To-day the accepted definition of a mycotic aneurysm is one due to septic infection in the wall of an artery; it is usually associated with bacterial endocarditis. The mode of formation of a mycotic aneurysm depends upon whether it is of the embolic or of the erosive type. If embolic, an infected embolus lodges in the vessel or in one of its vasa vasorum, and the inflammation, by weakening the arterial wall, causes it to give way with the formation of an aneurysm. If erosive, the inflammation spreads from the aortic valve or from a coarctation to the adjoining aorta, or, much less frequently, it comes from an extravascular source and weakens the vessel wall by spreading from the adventitia inwards.

In this paper we describe a case in which a mycotic aneurysm of the abdominal aorta developed owing to erosion of the aortic wall by tuberculosis of the pre-aortic lymph nodes.

Case Report

The patient was aged 59. Two months before admission to St. Mary's Hospital he noticed a pain in his back; this was a constant ache, worse at night, and was gradually getting more severe. He also suffered from pain in his calves and feet; this was worse when he stood up and relieved by rest in bed. He had occasional attacks of vomiting. Two weeks before admission he noticed a pulsatile swelling in his abdomen which was rapidly enlarging. He consulted Mr. A. Emlyn Williams at the Hampstead General Hospital, who considered that he had an aneurysm of the abdominal aorta and referred him to us for treatment.

He gave a past history of two bouts of pulmonary tuberculosis occurring respectively nine years and two years previously. Nine months before admission he had a cold abscess of the chest wall treated surgically at the Brompton Hospital. One of his brothers had died of pulmonary tuberculosis and one of his daughters also suffered from this disease.

On admission the scar of the operation on the chest wall was soundly healed and *x*-ray examination showed no evidence of an active pulmonary lesion. He was seen by Dr. W. D. W. Brooks, who considered that the pulmonary disease was quiescent. Examination of the abdomen revealed a slightly tender mass in the epigastrium situated just above and to the left of the umbilicus; this pulsated in an expansile manner and was considered to be an aneurysm of the aorta. Apart from a mild urinary infection, no other abnormality was detectable on clinical examination. Aortography (performed by Dr. David Sutton) demonstrated an aneurysm of the abdominal aorta between the renal arteries and the aortic bifurcation (Fig. 1).

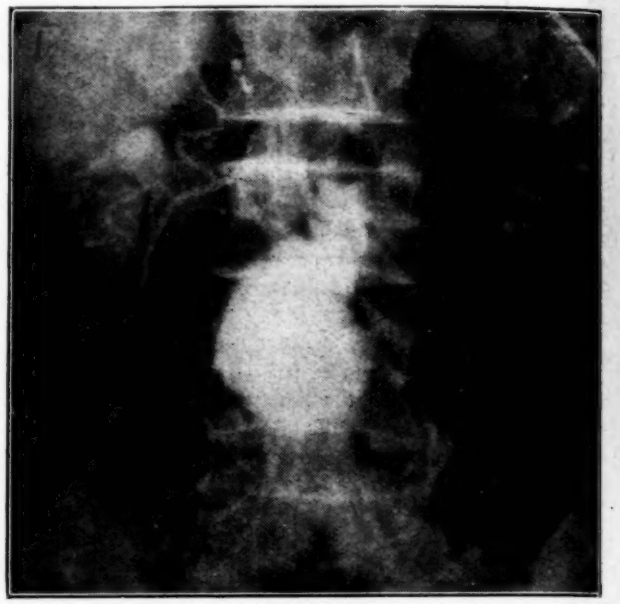

FIG. 1.—Pre-operative aortogram showing an aneurysm of the abdominal aorta.

At this stage the patient exhibited two unusual features as compared with the usual case of abdominal aortic aneurysm which we treat with a blood-vessel graft. He had an evening temperature of 100° F. (37.8° C.) and the aneurysm was unusually large clinically when compared with the size shown on the aortogram. The pyrexia was at first thought to be due to the urinary infection, but although this infection cleared with treatment the pyrexia persisted. In view of these findings and his previous medical history it was considered possible that he suffered from tuberculosis of the abdominal lymph nodes as well as an aneurysm of the aorta.

At operation a large mass of caseating tuberculous lymph nodes was found to be adherent to the anterior and lateral walls of an aortic aneurysm. At one point the aneurysm was very thin walled and about to rupture. The whole mass and the aneurysm were resected, the inferior mesenteric artery was tied, and continuity was restored by means of a prosthesis of "orlon" cloth. Orlon cloth was used in preference to an arterial homograft because the graft bed consisted in part of tuberculous tissue, and it was felt that this might spread and involve a graft.

The patient made a satisfactory recovery from the operation, and was discharged from hospital to a convalescent home one month later. There he completed a twelve-weeks course of streptomycin and P.A.S.

On examination of the specimen the resected portion of aorta was seen to have a moderate degree of atheroma; many enlarged caseating lymph nodes surrounded a saccular aneurysm. Microscopical examination demonstrated tuberculous granulation tissue with much central caseation abutting on the outer surface of the aorta, replacing the adventitia

and media in places, so that there was only thickened intima between the tuberculous tissue and the lumen of the aorta. In view of these findings we consider that this patient had a mycotic aneurysm of the abdominal aorta of the extravascular erosive type, the tuberculous disease in the lymph nodes having destroyed the adventitia and media of the aorta so that an aneurysm resulted.

Aortography performed one month after operation showed that there was good filling of the aorta, the orlon prosthesis, and the iliac arteries (Fig. 2). The patient has returned to work in his city office.

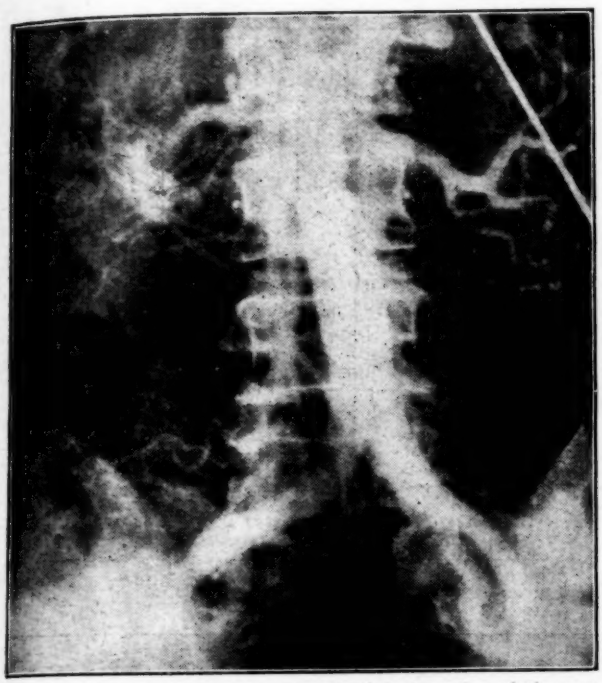

FIG. 2.—Post-operative aortogram showing the orlon cloth prosthesis in position.

Previous Reported Cases

In 1913 Haythorn reviewed the literature on tuberculosis of arteries and reported finding only one record of an aneurysm of the abdominal aorta due to erosion of the arterial wall by tuberculous granulation tissue. Since then occasional cases have been reported, and by 1933 Gellerstedt and Säfwenberg were able to collect 21 cases of aneurysm of the abdominal aorta due to erosion by tuberculous granulation tissue. The literature since 1933 contains reports of two more cases (Owens and Bass, 1944; Scott, Maxwell, and Grimes 1949), so it appears that, including our patient, only 24 cases of tuberculous mycotic aneurysm of the abdominal aorta have been recorded. Also, as the other reports were based upon material obtained at necropsy, ours is the first record of the diagnosis of this lesion with the subsequent recovery of the patient.

Summary

A case is reported of an aneurysm of the abdominal aorta due to erosion of the aortic wall by tuberculous granulation tissue from caseating abdominal lymph nodes. Treatment, which included resection of the aneurysm followed by reconstruction of the aorta with a prosthesis of orlon cloth, has enabled the patient to return to work.

Of 23 such cases previously reported in the literature, all were fatal.

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THE NUCLEIC ACID CONTENT OF BONE-MARROW CELLS IN PERNICIOUS ANAEMIA

BY

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The understanding of disordered processes of cell development has in the past depended mainly on the observation of morphological differences between cells at various stages of their life-cycle. By modern chemical and histochemical methods it is possible to analyse, in certain of the chemical constituents of cells, changes that are probably the underlying cause of alterations in morphology. The disordered cell development that occurs in pernicious anaemia is particularly worthy of study, for the cells are easily accessible, and, furthermore, the disease process is one that can be corrected by appropriate treatment. Of the therapeutic agents that restore the bone-marrow picture to normal, the most potent is vitamin B_{12}, which appears to be closely connected with the synthesis of nucleic acids that accompanies growth (Wright *et al.*, 1948; Rose and Schweigert, 1952). In spite of the fact that, from bacterial and animal experiments, much has been learned about the biological activity of vitamin B_{12}, very little is known of its mode of action in pernicious anaemia. There is as yet no real understanding of the nature of the cellular defect that is apparently remedied by vitamin B_{12}, but it seems possible that it may be a defect in nucleic acid metabolism.

It has been demonstrated that the deep basophilia of the cytoplasm of early megaloblasts is due to the presence of ribonucleic acid (Thorell, 1947; White, 1947); it has also been shown by chemical analysis that the mean amount of ribonucleic acid phosphorus (R.N.A.P.) per cell is much greater in megaloblastic marrows than in normal marrows (Davidson *et al.*, 1951). Accumulation of ribonucleic acid in the cell cytoplasm appears, therefore, to be a specific feature of megaloblastic haemopoiesis. That abnormalities may also occur in the cellular content of desoxyribonucleic acid (D.N.A.) was suggested by La Cour (1944), who, by histological methods, demonstrated chromosomal abnormalities in both the red-cell and the white-cell series in pernicious anaemia. The mean desoxyribonucleic acid phosphorus (D.N.A.P.) per cell is, in fact, greater in megaloblastic marrows than in normal marrows (Davidson *et al.*, 1951, 1953). On the other hand, it has been shown by microspectrophotometric techniques that the D.N.A. content of individual megaloblasts is no greater than that of normoblasts of comparable nuclear size (Reisner and Korson, 1951; Marinone, 1951).

In this paper we present the results of chemical estimations of the nucleic acid content of bone-marrow cells in pernicious anaemia, and make an attempt to assess the significance of the findings, particularly with regard to the cellular content of D.N.A.P. Quantitative changes in nucleic acids during *in vitro* culture will be described elsewhere.

Experimental Work

Estimations of nucleic acids were carried out on suspensions of blood or bone marrow containing a known number of nucleated cells per cubic millimetre, thus enabling the mean amount of nucleic acid per cell to be calculated. Sternal marrow samples were taken from 18 patients suffering from classical pernicious anaemia, and the series of observations has been compared, not with normal marrows, but with observations on nine bone marrows showing normoblastic hyperplasia. Cases in the latter group were selected because the clinical and bone-marrow findings suggested that the erythroid elements of the marrow might be functioning near their maximum capacity, which would cause the marrow aspirates to contain a high proportion of "active" cells. The use of such cases was thought to afford a better comparison between megaloblastic and normoblastic haemopoiesis than the use of normal subjects, from whom marrow aspirates contain a high proportion of mature leucocytes. In addition, seven samples of normal blood were examined.

Technique

Blood samples of approximately 3 ml., obtained by venepuncture, were collected in bijou bottles containing as an anticoagulant the standard mixture of ammonium and potassium oxalate. Sternal marrow puncture was performed by the standard technique, employing a Salah sternal puncture needle and an all-glass syringe, both siliconed. When approximately 1 ml. of the blood-and-marrow mixture had been aspirated, the syringe was quickly detached from the needle and its contents were ejected into 20 ml. of normal saline in a universal container. Although anticoagulants were not used, it was found that if the mixture of marrow and saline was shaken for 20 minutes clotting did not occur. After centrifugation for five minutes, the fatty debris was taken from the top of the liquid and the supernatant fluid removed by Pasteur pipette until about 2 ml. remained. Agitation then produced an even cellular suspension, on which three independent nucleated cell counts were made.

Nucleic acids were estimated as nucleic acid phosphorus (N.A.P.) by the technique described by Davidson *et al.* (1949), in which the D.N.A.P. and R.N.A.P. fractions are separated by the method of Schmidt and Thannhauser (1945). The amount of inorganic phosphorus present in the two fractions was measured by the colorimetric method of Berenblum and Chain (1938). Readings were taken on a calibrated Unicam spectrophotometer, and by this technique satisfactory measurement was obtained of quantities of phosphorus between 0.5 and 4 μg.

Results

In Table I, II, and III are recorded the mean values of nucleic acid phosphorus per cell found in normal leucocytes, in cells from bone marrows undergoing active normoblastic hyperplasia, and in cells from the bone marrow of patients suffering from pernicious anaemia. No figures are recorded for the mean amount of R.N.A.P. per leucocyte, because difficulty was experienced in extracting all the acid-soluble phosphorus compounds from whole blood, thus making the R.N.A.P. figures unreliable.

The mean value for the cellular content of R.N.A.P. is higher in the pernicious anaemia series than in the normoblastic ($t=2.548$; $n=19$; $P<0.02$); this finding is consistent with the observations that the early megaloblasts present in the marrow of pernicious anaemia are unusually rich in R.N.A. (White, 1947; Thorell, 1947). The distribution of the individual D.N.A.P. results in each series is depicted in the Chart, and the grand means are compared in Table IV. The lack of a significant difference between the marrow cells

TABLE I.—*Mean D.N.A.P. of Normal Blood Leucocytes*

Case No.	Mean D.N.A.P. per cell in $\mu g. \times 10^{-7}$
30	5·67
31	5·37
32	5·39
37	5·70
44	6·92
45	5·90
46	6·31

Mean = $5·89 \times 10^{-7}$ $\mu g.$

TABLE II.—*Mean Cellular Content of D.N.A.P. and R.N.A.P. in the Bone Marrow of Patients in whom Clinical and Bone-marrow Findings Indicated the Presence of Active Blood Regeneration*

Case No.	Age and Sex	Diagnosis	Hb g./ml.	R.B.C. in mills./c.mm.	Retics. %	W.B.C. per c.mm.	D.N.A.P. $\mu g. \times 10^{-7}$ per cell	R.N.A.P. $\mu g. \times 10^{-7}$ per cell
2	18 M	Acholuric jaundice	12·9	4·2	10·3	8,900	7·0	15·5
8	65 M	Paroxysmal nocturnal haemoglobinuria	6·2	1·3	11·4	9,000	6·2	—
17	23 M	Familial haemolytic anaemia	10·8	3·3	13·1	5,400	9·8	4·8
19	73 F	Cancer of bladder Haematuria ++	7·6	2·4	—	6,050	8·8	5·4
25	61 F	Acholuric jaundice	8·6	3·0	30·4	4,200	6·2	14·5
27	35 F	" "	11·3	4·5	10·4	16,200	8·9	16·0
34	51 M	Acquired haemolytic anaemia	3·5	0·8	60·6	11,350	5·1	—
41	51 M	Acholuric jaundice	12·9	4·2	4·4	10,050	8·6	7·3
22	48 F	Chronic haemolytic anaemia	10·1	3·5	6·2	7,600	16·0	11·3

Grand mean D.N.A.P. per cell = 8.51×10^{-7} $\mu g.$ Grand mean R.N.A.P. per cell = 10.69×10^{-7} $\mu g.$

TABLE III.—*Mean Cellular Content of D.N.A.P. and R.N.A.P. in the Bone-marrow of Pernicious Anaemia*

Case No.	Age and Sex	Hb g./ml.	R.B.C. mills./c.mm.	D.N.A.P. $\mu g. \times 10^{-7}$ per Cell	R.N.A.P. $\mu g. \times 10^{-7}$ per Cell
1	41 M	7·7	1·93	5·8	10·8
9	61 F	9·2	2·05	6·25	—
10	58 F	7·7	1·77	7·5	—
14	38 F	3·7	1·10	6·65 (7·2, 6·1)	5·6
15	65 M	5·0	1·10	5·7 (6·7, 6·5, 4·0)	28·2 (32·8, 40·2, 11·5)
18	76 M	5·9	1·36	6·7	20·0
20	58 M	8·6	2·18	10·2 (10·6, 8·6, 11·4)	22·1 (23·0, 17·3, 26·0)
23	54 F	7·4	1·63	10·45 (11·2, 9·7)	20·3 (20·0, 20·6)
24	62 F	8·3	2·11	10·5 (8·6, 11·1, 11·8)	12·2 (14·0, 11·1, 11·6)
26	44 F	6·8	1·51	13·0 (12·1, 13·9)	27·3 (27·2, 27·5)
28	69 M	8·0	1·82	16·1	28·6
29	64 M	4·7	1·07	8·3 (10·9, 5·7)	24·3 (25·6, 23·0)
35	67 F	7·0	1·59	6·1	11·7
36	41 M	5·3	1·40	14·6	—
38	63 F	6·8	1·41	4·5 (5·9, 3·0)	12·7 (16·2, 9·2)
39	68 F	8·4	1·94	7·1	—
42	42 F	5·0	1·07	12·9	14·7
43	38 F	6·7	1·56	6·9 (6·9, 7·1, 6·8)	20·9 (21·5, 19·2, 22·0)

Figures in parentheses are individual results in cases in which estimations were carried out on more than one marrow suspension from the same patient. Clearly, the wide range of nucleic acids in pernicious anaemia is due, not entirely to experimental error, but mainly to a real case-to-case difference.

Grand mean D.N.A.P. per cell = 8.85×10^{-7} $\mu g.$ Grand mean R.N.A.P. per cell = 18.53×10^{-7} $\mu g.$

TABLE IV.—*Comparison of the Mean Nucleic Acid Phosphorus Per Cell in Blood and Bone-marrow Cells (Numbers of Cases in Parentheses)*

	A	B	C
	Blood Leucocytes	Active Normoblastic Marrow	Pernicious Anaemia Marrow
D.N.A.P. as $\mu g. \times 10^{-7}$/cell	5·89 (7)	8·51 (9)	8·85 (18)
R.N.A.P. as $\mu g. \times 10^{-7}$/cell	—	10·69 (7)	18·53 (14)

The difference between the D.N.A.P. means in A and B is not significant ($t=2.116$, $n=14$, $P=0.053$); that between the means in A and C is of borderline significance ($t=2.258$, $n=23$, $P=<0.05$). The R.N.A.P. mean of C is greater than that of B ($t=2.548$, $n=19$, $P=<0.02$).

as compared with leucocytes is due to the relatively small numbers in two of the three series, but the present object is not to demonstrate such a difference but rather to compare the bone marrow of pernicious anaemia with that of active normoblastic hyperplasia. The results indicate that the cellular content of D.N.A.P. is quantitatively similar in these two types of bone marrow.

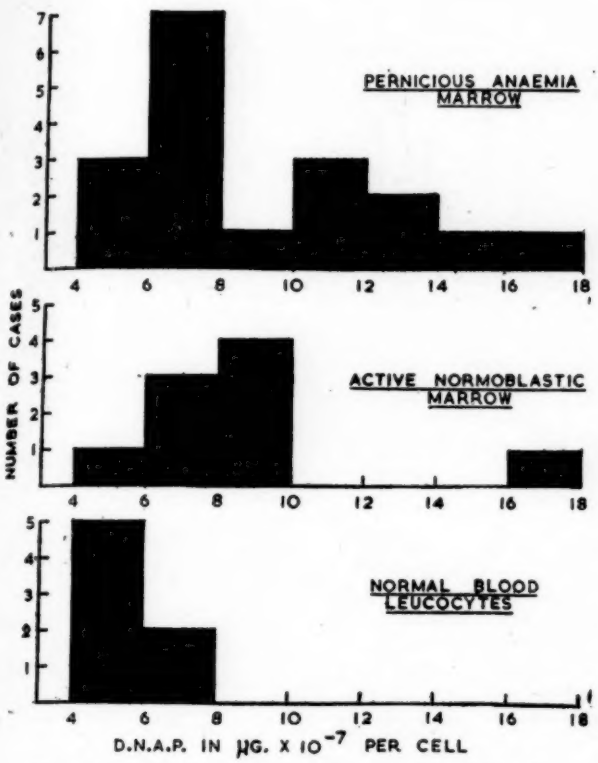

Chart showing the mean cellular content of D.N.A.P.

Discussion

Appreciation of the significance of the results depends on a knowledge of the role of D.N.A. in the life of the cell, in which it forms an essential part of nuclear chromatin (Brachet, 1933). A considerable amount of evidence points towards the idea that, in any given genus, the mean content of D.N.A. per mature diploid cell is constant, being twice that of the haploid sperm (Boivin *et al.*, 1948; Vendrely and Vendrely, 1948, 1949; Mandel *et al.*, 1950; Davidson *et al.*, 1951).

During cell proliferation, changes must of course occur, and these have, in recent years, been studied intensively by a number of workers using quantitative spectrophotometric techniques that enable the D.N.A. content of individual cells to be estimated. It has been shown that D.N.A. increases during interphase until at prophase twice as much is present as in the non-dividing cell; hence daughter nuclei have the normal complement of D.N.A. (Swift, 1950; Pasteels and Lison, 1950; Walker and Yates, 1952). Thus if the mean amount of D.N.A. per cell in a population is high it may be presumed that a high proportion of cells are of actively dividing type, or that mitotic abnormalities have occurred, resulting in polypoid cells, or that some fundamental abnormality exists in the chromosomal content of D.N.A.

The blood leucocyte is a good example of a mature non-dividing diploid cell, and the results recorded in Table I indicate that in normal subjects the mean amount of D.N.A.P. per leucocyte is remarkably constant. Moreover, as the results are in agreement with published figures for the D.N.A.P. content of other mammalian cells (Table V), they lend support to the theory of constant D.N.A. per cell.

Tables II and III demonstrate the wide variability that occurs between different bone marrows as regards the mean

TABLE V.—*Mean D.N.A.P. Content of Various Mammalian Cells. D.N.A.P. as μg.×10⁻⁷ Per Cell. (Figures Published as D.N.A. Have Been Multiplied by* 0.099.)

Author	Normal Sperms	Normal Leucocytes	Other Mature Cells*	Normal Marrow	Active Normoblastic Marrow	Megaloblastic Marrow
Boivin *et al.* (1948)	3·37	—	6·43	—	—	—
Mirsky and Ris (1949)	2·79	—	6·14 to 8·37	—	—	—
Mandel *et al.* (1950)	—	6·78	—	—	—	—
Davidson *et al.* (1951)	3·14	7·04	8·3 to 10·0	8·69	—	12·7
Present	—	5·89	—	—	8·51	8·85

* Cells from liver, kidney, etc. (may include some dividing cells).

content of D.N.A.P. per cell, a finding that has also been observed by Davidson *et al.* (1951) and by Menten and Willms (1952). In a series of 31 cases showing a preponderance of erythroblasts in bone-marrow smears, the latter authors found values of D.N.A.P. per cell ranging from 4.0 to 26.3 × 10^{-7} μg. Included in their series were six cases of pernicious anaemia, the mean value for those being 16.0 × 10^{-7} μg./cell. Values higher than the present figure of 8.81 were also found by Davidson *et al.*, who in 17 cases of megaloblastic marrows reported a mean value of 12.7 × 10^{-7} μg. D.N.A.P. per cell. However, the latter figure represents approximately 180% of their mean value of D.N.A.P. per leucocyte (7.04), whereas the mean of the present series represents 150% of the present leucocyte value, so that differences between the present results and those of Davidson *et al.* probably depend on technique and may not be of great significance. Other important findings of Davidson *et al.* were that the mean content of D.N.A.P. per cell in megaloblastic marrows was higher than in normal marrows, marrows from cases of leukaemia, or marrows of iron-deficiency anaemia. Those authors considered that the high values in their megaloblastic series indicated the presence of nuclear abnormality, either polyploidy or polyteny. Such a theory is in agreement with the frequent finding of abnormal mitotic figures in megaloblastic marrow smears and with the suggestion, made by La Cour (1944), that tetraploid cells are common in the bone marrow of pernicious anaemia.

The present results, although they do not in any way invalidate the theory of nuclear abnormalities, are more in favour of the alternative hypothesis that the high cellular D.N.A.P. of the pernicious anaemia marrow is due to the presence of proliferating cells. In the hyperplastic normoblastic marrows a considerable amount of cellular multiplication was going on, and the figures for the mean cellular D.N.A.P. must depend on the fact that there was a mixed population of cells, some containing the diploid quantity, others containing an excess of D.N.A.P. in preparation for mitosis. The mean content of D.N.A.P. per cell for the whole series of pernicious-anaemia marrows is similar to that of the normoblastic series, which suggests that the same factors may have operated in each case.

Thus it would appear that the high cellular content of D.N.A.P. encountered in the bone marrow in pernicious anaemia may be due, not to some specific abnormality of mitoses, but to the prevalence in the marrow of cells of proliferative type.

Summary

Chemical estimations of nucleic acids have been carried out on suspensions of blood and bone-marrow cells.

The cellular content of R.N.A.P. is higher in pernicious-anaemia marrows than in hyperactive normoblastic marrows; accumulation of R.N.A. in the cell is therefore a specific feature of megaloblastic haemopoiesis.

The cells of pernicious-anaemia marrows and those of hyperactive normoblastic marrows contain approximately the same amount of D.N.A.P., the figures in each

case being about 150% of values for blood leucocytes. This finding suggests that many of the cells of the pernicious-anaemia marrow are of proliferative type and are engaged in building up D.N.A. in preparation for mitosis.

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CEREBROVASCULAR ACCIDENTS IN HOSPITALS FOR ACUTE CASES

BY

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Patients with intracranial vascular lesions, especially those over 70, are a serious problem to the general practitioner called upon to arrange suitable care and accommodation. Hospitals are unwilling to admit cases likely to remain as chronic hemiplegics occupying acute medical beds for long periods. Those who do get admitted are often accepted with reluctance after tedious negotiations which are irritating to both house officers and practitioners. The attitude of hospital staffs would be easier to defend if it were not based as much on traditional prejudice as on an appreciation of what actually happens to these cases after admission.

This paper reports an analysis of 239 cases admitted after cerebrovascular accidents in which the length of stay in hospital and the eventual disposal have been investigated.

Material and Methods

The in-patient records of two hospitals were examined for the two-year period 1948–9. Extracts of age, sex, length of stay, and disposal were made of all cases admitted with the diagnoses of cerebral haemorrhage, thrombosis and embolism, subarachnoid haemorrhage, hemiplegia, and coma of unknown cause. The 239 cases collected were analysed with respect to length of stay in hospital by age and sex. The duration of symptoms before admission was not studied in detail, but only three of the cases were admitted as long-standing hemiplegias and the majority were victims of recent cerebrovascular accidents.

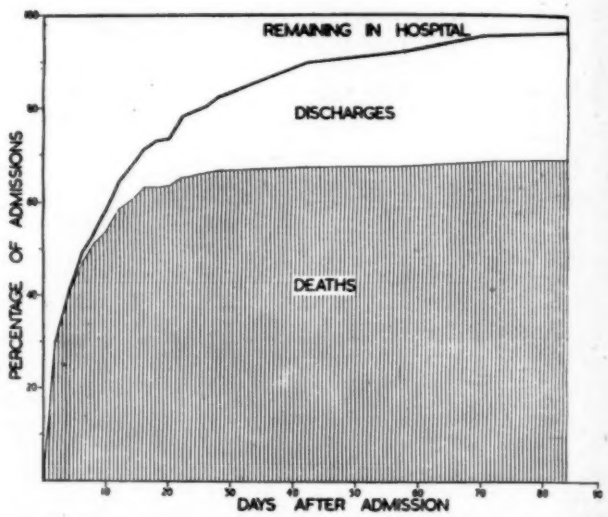
The two hospitals selected are situated in a large industrial county town in the midlands of England. Hospital A is an ex-voluntary hospital of over 600 beds with a casualty department. Hospital B is an ex-municipal hospital of 400 beds with no casualty department. Between them the two hospitals accommodate most of the acute medical admissions from a population of 600,000.

Results

Table I summarizes the patients with intracranial vascular lesions admitted to the two hospitals. Of the 239 patients 165 (69%) died in hospital and 74 (31%) were discharged. Of the discharges 61 (25.5% of admissions) were sent home, and 13 (5.4% of admissions) were transferred to other hospitals.

TABLE I.—*Summary of 239 Cases with Intracranial Vascular Lesions Admitted to Hospital in 1948–9*

	Hospital A			Hospital B			Total		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
Discharged home ..	10	17	27	12	22	34	22	39	61
Transferred	6	3	9	4	—	4	10	3	13
Died ..	34	55	89	27	49	76	61	104	165
Total ..	50	75	125	43	71	114	93	146	239



Cumulative frequency diagram showing the percentage of patients remaining in hospital, discharged, or dead after a given period of time.

The length of stay in hospital is shown in the form of a cumulative frequency diagram. Over 30% of admissions died in the first two days. By the end of 10 days 54.2% had died and 5% had been discharged, leaving 40.8% still in hospital. After six weeks 67.6% had died, 21.8% had been discharged, and 10.6% remained. Only 3.8% stayed in hospital more than 12 weeks.

Table II gives the length of stay in hospital according to age. Of those over 60 years old 10 out of 141 (7.1%) stayed in more than six weeks, compared with 14 out of 98 (14.3%) of those under 60. The difference between these percentages is not significant. The number of deaths in the higher

TABLE II.—*Length of Stay in Hospital According to Age. Discharges by Death are Given in Parentheses*

Week of Discharge	Age Group						
	20–29	30–39	40–49	50–59	60–69	70–79	80–89
1–2	3 (2)	3 (3)	16 (13)	35 (28)	58 (54)	40 (37)	8 (8)
3–4	—	1	7 (2)	10 (3)	8 (3)	6 (4)	2 (2)
5–6	—	1	6	2	5 (2)	4	—
7–8	—	—	1	3	1	—	—
9–10	—	1 (1)	1	3 (1)	3 (1)	—	1
11–12	—	—	—	—	1 (1)	—	—
Over 12	—	1	—	4	3	1	—
Total	3 (2)	7 (4)	31 (15)	57 (32)	79 (61)	51 (41)	11 (10)

age groups is, however, significantly greater than in the younger groups ($\chi^2=21.53$; df=6 ; P<0.001).

Table III shows the percentage of medical beds occupied by patients with intracranial vascular lesions. The number of beds occupied by chronic cases, those who have been in

TABLE III.—*Percentage of Medical Beds Occupied by Intracranial Vascular Lesions*

	Men		Women	
	Hospital A	Hospital B	Hospital A	Hospital B
All cases	1·47	2·13	3·07	4·08
Cases in hospital more than:				
2 weeks	0·51	1·26	1·53	2·62
4 ,,	0·26	0·73	0·93	1·87
6 ,,	0·18	0·45	0·59	1·26
8 ,,	0·14	0·29	0·37	1·01
10 ,,	0·10	0·17	0·27	0·77
12 ,,	0·06	0·14	0·17	0·59

hospital more than a given time, is also indicated. From this table can also be estimated the proportion of beds saved by transfer of cases after, say, three or four weeks to a special hemiplegic unit.

Discussion

It is surprising to find that less than 5% of patients with intracranial vascular lesions became chronic hospital patients, and these occupied only a small proportion of the total medical beds. Patients over 60, because of the high mortality in this group, were not especially liable to become chronic cases. In fact, it was the younger groups which provided the largest number of long-term cases, probably owing to their greater ability to survive grossly disabling lesions.

The most striking feature of this series was the extremely high death rate in the first few days after admission. The expectation of survival increased rapidly with the age of the lesion. Hospitals which accept early cases, particularly those with casualty departments where patients with sudden apoplexy are taken from the street, can expect a large intake, a high mortality, and a rapid turnover, with relatively few chronic survivors. Those which accept late cases will have a smaller intake, a low mortality, and a long average stay in hospital. For this reason the experience of some hospitals may differ considerably from the two which have been studied in this investigation. What the present series does show is that a generous acceptance of early cases is not necessarily followed by an accumulation of chronic hemiplegics.

There are good reasons why cerebrovascular accidents should be admitted to hospital as soon as they occur, irrespective of the age of the patient or other social factor. Rehabilitation must be started early if it is to prevent permanent disability from contractures (Rusk and Taylor, 1952). Old people must be forced to help themselves before they become reconciled to a life of bed-fast dependence. Such treatment is more effectively carried out in hospital than in the patient's own home. Denial of hospital facilities in these circumstances is likely to add to the number of helpless cases at large in the community, and in the long run actually increase the demand for their accommodation in beds for acute cases.

Summary

The hospital records of 239 cases admitted to hospital following cerebrovascular accidents have been examined.

Less than 5% remained in hospital more than three months. Patients over 70 were not especially liable to become chronic hemiplegics.

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VALUE OF SERUM IRON LEVELS IN ASSESSING EFFECT OF HAEMATINICS IN THE MACROCYTIC ANAEMIAS

BY

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The serum iron shows specific variations in different types of anaemia (Riecker, 1930 ; Powell, 1944 ; Laurell, 1947 ; Cartwright and Wintrobe, 1952). It is low when the cause is iron deficiency, infection, or malignancy. Higher values than normal usually occur in the macrocytic anaemias and in those due to haemolysis or hypoplasia of the bone marrow. Moore and Doan (1937) reported two cases of pernicious anaemia in which the initial high figures of serum iron fell to a low level during a remission. The following is a study of the variations of serum iron before and after treatment in the macrocytic anaemias. It was thought that a definite correlation between an early fall in serum iron and effective therapy might provide a quick and simple method of assessing the effect of a haematinic in the macrocytic anaemias.

Material and Methods

Macrocytic anaemias of all types, such as pernicious anaemia, the sprue syndrome, liver disease, and pregnancy, were studied. The patients were treated by an injection of a haematinic, usually vitamin B_{12} or folic acid, in hospital. The response in the blood was measured by the rise in erythrocytes after 15 days (Ungley, 1949) and by the reticulocyte count.

The blood for serum iron estimation was always taken at about 10 a.m. to avoid errors due to the diurnal variation (Vahlquist, 1941 ; Hoyer, 1944 ; Hamilton *et al.*, 1950). Modern methods for serum iron determination (Laurell, 1947 ; Vannotti and Delachaux, 1949) are simple and accurate. A fastidious cleanliness is needed, as iron is a common contaminant ; so that all-glass syringes and specimen tubes, dry sterilized and specifically cleaned, are used for taking samples of blood. The following technique, adapted by P. W. Perryman (1948, personal communication), has been used.

In a centrifuge tube is placed 4 ml. of serum, to which 1 ml. of 6 N HCl is added, mixed well, and left to stand for ten minutes. Then 3 ml. of 20% trichloracetic acid is added, stirred with a glass rod, left for 5 minutes, and centrifuged at high speed for approximately 20 minutes. (A longer period may be necessary if particles are still present when the supernatant fluid is drawn off.) Then 4 ml. of supernatant fluid is placed in a glass-stoppered tube and approximately 50 mg. of ascorbic acid added and the solution left for 10 minutes, with occasional shaking to encourage the ascorbic acid to dissolve. Finally, 0.5 ml. of $\alpha\alpha$-dipyridyl in 0.1 N HCl, or 1 ml. of 0.1% orthophenanthroline, and 0.5 ml. of concentrated ammonia solution, are added. The tubes must be agitated well immediately on adding these last two solutions. 1 ml. of doubly distilled water is added to bring the final solution to 6 ml. for the cell of the spectrophotometer (Unicam, S.P.500). The blank consists of 3 ml. of doubly distilled water, 0.5 ml. of 6 N HCl, 1.5 ml. of 20% trichloracetic acid, then ascorbic acid, reagent, and ammonia solution as above.

Calibration curves were prepared by making known solutions of ferrous ammonium sulphate, through the range of 50 to 500 μg. per 100 ml., and putting them through the same process as for serum. If, for other reasons, it is desirable to avoid using strong ammonia in the laboratory,

0.5 ml. of saturated sodium acetate can be used as a buffer instead; for this, the serum is incubated at 37° C. for one hour with 2 ml. of 0.3 N HCl, then 2 ml. of 20% trichloracetic acid is added, and the solution left for one hour. Otherwise there is no change in the technique. All the glassware is washed, left in cleaning fluid (potassium dichromate 100 g., sulphuric acid conc. 800 ml., water 1,200 ml.), washed thoroughly again in running tap-water, then rinsed in distilled water. All the reagents must be chemically pure, and made in doubly distilled water.

The standard deviation of a single determination from the mean, calculated from 42 duplicate analyses, was ±3.05 μg. per 100 ml. of serum. Seventy-four samples were analysed from 48 normal males and 26 normal females. The mean serum iron concentration was 126.8 μg per 100 ml. (S.D. 30), and the values ranged from 71 to 205 μg. per 100 ml. The mean serum iron for males was 130.8 μg. per 100 ml. (S.D. 30.8); for females, 119.4 μg. per 100 ml. (S.D. 27).

Results

The serum iron was studied before and after therapy on 100 occasions. In 60 the treatment was effective, and in every case the serum iron fell to a low figure during the remission. In 40 the haematinic was ineffective and the serum iron remained within similar limits. The fall in serum iron after successful treatment is striking and abrupt (Fig. 1). It was next determined how soon this took place,

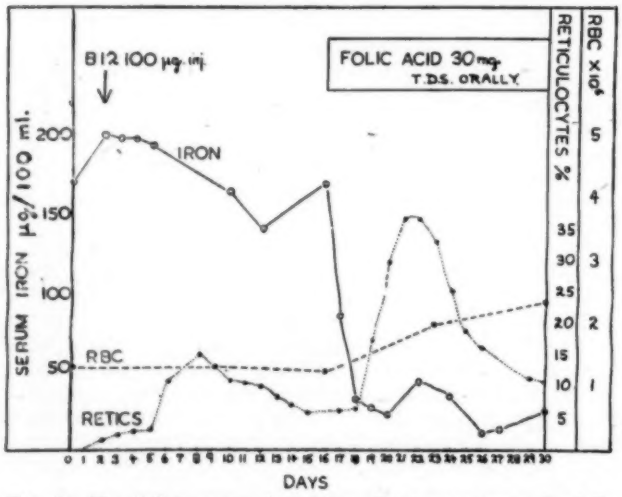

FIG. 1.—The fall in serum iron after effective treatment by folic acid in a case of megaloblastic anaemia of unknown origin.

and the earliest reliable time to estimate this change. To six patients with pernicious anaemia an injection of 100 μg. of vitamin B_{12} was given, and readings were taken at two-hourly intervals for eight hours; a significant fall occurred in one only. However, at 24 hours a significant change was obvious in 21 out of 23 cases; in the two with little or no change a further figure at 48 hours showed the characteristic fall. It was thereafter decided to rely upon the 48-hour reading of the serum iron.

The 48-hour reading of the serum iron has been studied on 33 occasions, and the change correlated with the result of therapy in every instance except one, a case of steatorrhoea in which a submaximal reticulocyte response occurred after vitamin B_{12} without any rise in the red blood cells. Here the fall was transient and returned to normal within the week. The maximum change was 228 μg per 100 ml. (from 278 to 50 μg. per 100 ml.), and the minimum significant fall was 20 μg. per 100 ml. (from 46 to 26 μg. per 100 ml.); the mean was 105 μg. per 100 ml. Whatever the initial height of serum iron, the values tended to fall to about the same level (Fig. 2); they then remained at about 50–60 μg. per 100 ml.—unaffected by the reticulocyte response—until the blood count returned to normal. Insufficient dosage of the haematinic was shown by the serum iron rising to the previous levels. Impending iron deficiency was indicated by a fall to a lower level; values below 40 μg. per 100 ml. were suggestive, and below 30 μg. per 100 ml. diagnostic of this. The mean of nine cases at one week that later developed iron deficiency was 27.3 μg. per 100 ml. (range from 11 to 39 μg. per 100 ml.). This often preceded the signs of iron deficiency in the blood count by several weeks.

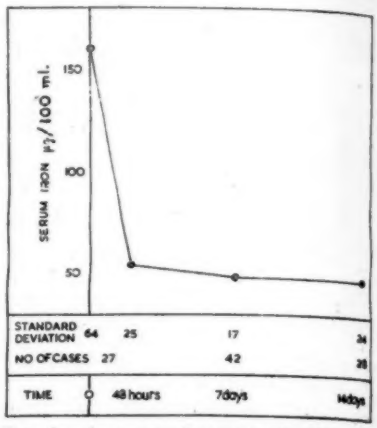

FIG. 2.—A composite graph showing the fall in serum iron following effective therapy in cases of macrocytic anaemia.

The total iron-binding capacity (Cartwright and Wintrobe, 1949) was measured on five occasions before and after successful therapy. There is no significant change unless iron deficiency develops, when the typical high figures are seen. Twelve normal controls were given injections of vitamin B_{12} or folic acid, and no change took place in the serum iron or total iron-binding capacity.

Discussion

The 48-hours serum iron test is a reliable method of assessing the effect of haematinics in the macrocytic anaemias. A fall in the serum iron is probably the earliest sign of a haematological response, for the bone-marrow reversion is not complete until 32 to 72 hours (Davidson *et al.*, 1942), and the reticulocyte response does not appear for several days. The test is useful if the level of the initial red-cell count is such (3,000,000 cells per c.mm. or more) that the reticulocyte change is slight or inconclusive, and in out-patient trials where the patient cannot attend daily for reticulocyte counts. It is helpful in severely ill patients, in whom the earliest indication of effective therapy is needed, as waiting may be dangerous. It is probably unaffected by a blood transfusion being given at the same time as the haematinic. It is the first sign of impending iron deficiency. It is not necessarily suggested that this test should be used for routine clinical work, as the reticulocyte response and the rise in red cells are already sufficient. However, the study of the macrocytic anaemias and their response to various haematinics is becoming a complex problem, and it may be that a simple test, with a precise and sharp end-point, will be of value.

The explanation of the fall to a low level is perhaps that the rate of release of iron from the stores, possibly by enzymic action, cannot keep pace with the increased demand. It is interesting that, irrespective of the initial height, the level after successful therapy is similar in all. This figure may represent a state of physiological balance between the stores and the bone marrow. The test is an index of an increased turnover of iron in the body, and the low serum iron a measure of erythropoietic activity.

Summary

A test for assessing the effect of haematinics in the macrocytic anaemias is described.

The fall in the serum iron is the first sign of effective therapy.

The level of the serum iron gives the earliest indication of impending iron deficiency.

I am grateful to our deputy biochemist, Mrs. R. M. Lainchbury, for doing the serum iron estimations, and to my colleagues

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IRON DEFICIENCY IN PREGNANCY

BY

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Some fall in the level of haemoglobin during pregnancy is usual. This relative anaemia is often attributed to the rise in blood volume of 18–23% (Dieckmann and Wegner, 1934; Roscoe and Donaldson, 1946; Berlin *et al.*, 1953) which occurs towards the end of pregnancy. Since the haemoglobin levels of most non-pregnant women range from 80 to 95%, levels of haemoglobin of 70–85% at the end of pregnancy have come to be accepted as normal.

The fact that throws doubt on the "physiological" nature of the anaemia of pregnancy is that the anaemia can in most cases be prevented by the administration of iron (Corrigan and Strauss, 1936; Fullerton, 1936; Wills *et al.*, 1947; Klopper and Ventura, 1951; Scott and Govan, 1949; Benstead and Theobald, 1952; Davis and Jennison, 1954).

The present investigation does little more than confirm this finding, but it was thought that our evidence should be added to that already available both because low haemoglobin levels in pregnancy are undesirable and because there is a continuing failure to recognize that they are unnecessary.

Plan of the Present Investigation

The investigation was carried out on patients booked for domiciliary delivery and attending two local health authority antenatal clinics between January, 1951, and April, 1953. All patients presenting themselves before the end of the fourth month of pregnancy were included. The haemoglobin levels were measured by the M.R.C. neutral grey photometer, taking 100% haemoglobin to be equivalent to 14.8 g.% of haemoglobin. Haemoglobin estimations were made at the first attendance, at 28 weeks, at 38 weeks, and six weeks after delivery. These dates are approximate, and occasionally the post-natal reading was at a rather later date.

Every patient was given an iron preparation by mouth from the time of first attendance until delivery. This was given in the form of one "fersolate" tablet (containing 3 gr. (0.2 g.) of ferrous sulphate) three times a day. The preparation was changed to "ferro-redoxon" (containing 2.04 gr. (132 mg.) ferrous sulphate and 50 mg. of ascorbic acid) if the patient complained of digestive disturbances or if the haemoglobin level had not risen. This change was made in about half the cases, and it appeared that the preparation containing ascorbic acid was better tolerated. The main difficulty in satisfactory iron therapy during pregnancy is that patients who feel well cannot be relied on to take it regularly, partly because any minor discomfort is attributed to it and partly because they see no necessity for it. We explained that taking iron regularly would make them feel "fighting fit" for their labour and also for their return to household duties after the lying-in period. In general this produced ready co-operation. At every attendance the patient was given the exact number of tablets to cover the period till she was due to come again and was asked to bring back the box with any that were left. These were counted and the number was recorded. It is clearly impossible to be certain that all the tablets not returned were consumed, but we felt that the record was as accurate as it could be, short of seeing the tablets swallowed.

The investigation included 138 patients. Of these, five could not be persuaded to persevere with iron and were excluded. In 26 instances the complete set of haemoglobin estimations was not obtained, either because the baby arrived before the calculated date, so that the 38-week reading was not made, or because the patient removed from the district or was transferred to the care of a hospital or general practitioner. Three further patients were excluded because they were given blood transfusions after post-partum haemorrhage. The 104 remaining cases are listed according to age and parity in Table I. There were no complications of pregnancy or labour in these patients apart from three forceps deliveries.

TABLE I.—*Age and Parity of* 104 *Women who Took Iron Regularly During Pregnancy*

Age	Parity					
	0	1	2	3	4	5
Under 20 ..	3	—	—	—	—	—
20–29	14	18	11	6	1	—
30–39	1	9	12	17	6	1
40 or over ..	—	—	3	1	1	—
Totals ..	18	27	26	24	8	1

Results

A difficulty in the analysis of the results of this survey is that a few patients failed to respond to iron therapy. We have isolated as a separate group all those in whom the haemoglobin level was still below 85% at 38 weeks and have termed them "non-responders." Table II shows the distribution of haemoglobin levels before the end of the fourth month of pregnancy in both "responders" and "non-responders" and indicates that there is no systematic difference in this respect between the two groups.

TABLE II.—*Haemoglobin Levels Before the End of the Fourth Month of Pregnancy in* 104 *Patients who Took Iron Regularly*

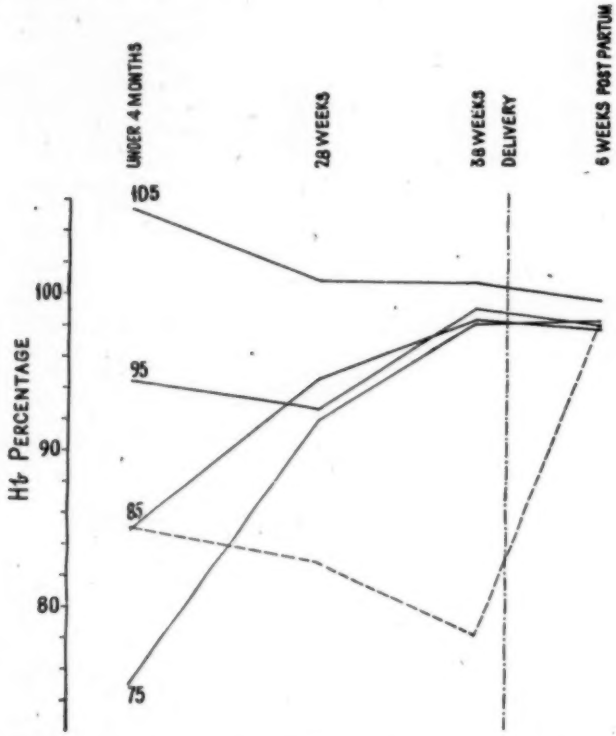
	Hb Levels				Total
	80% or Less	81–89%	90–99%	100%+	
Responders ..	15	33	33	11	92
Non-responders	4	3	5	0	12

Note.—Statistical examination of the age and parity of the responders does not show any significant difference between the four groups.

The effect of iron on the haemoglobin level is illustrated in the chart, where the "responders" have been subdivided according to their initial haemoglobin. This shows that when the initial haemoglobin is below 90% the administration of iron leads to a marked rise during pregnancy. When the initial haemoglobin is above 90% there is little systematic change in the level. In all the "responding" groups the haemoglobin level is around 98% at 38 weeks and remains at much the same level for six or more weeks after delivery. The "non-responders," who show a general downward trend

in haemoglobin levels from 16 to 38 weeks, show a sharp post-partum rise to the same level as all the "responding" groups.

It is to be noted that very little effect on the form of the curves would be produced if the "non-responding" cases were included in the appropriate subclasses of "responders." In general the curves would be not more than 2% lower at 28 weeks, not more than 4% lower at 38 weeks, and unaltered post partum.



Change in mean haemoglobin level in pregnant women receiving iron. The line marked 75 gives mean values for 15 patients whose haemoglobins were initially 80% or under. That marked 85 refers to 33 patients starting between 81 and 89%. Similarly, 95 denotes the range 90-99% (33 patients) and 105 denotes initial levels from 100% upwards (11 patients). The interrupted line refers to the 12 patients classified as "non-responders."

Discussion

The results of this investigation suggest that patients whose haemoglobin levels are below 90% at the beginning of pregnancy are iron-deficient, since the level rises steeply when they are treated with iron. The patients whose haemoglobin level is over 90% at the beginning of pregnancy maintain their high level at 38 weeks when treated with iron. Thus the steady fall in haemoglobin repeatedly reported to be characteristic of pregnancy—for example, M.R.C. (1945)—does not occur if iron is administered, except in the small group of "non-responders." Moreover, the level of haemoglobin at 38 weeks is almost the same as that observed six weeks or more after delivery—again with the exception of the few "non-responders." This finding appears to dispose of the idea that a fall in haemoglobin as pregnancy proceeds is due to haemodilution and is therefore "physiological." It is possible that this process may occur in the "non-responders," in view of the sharp rise that they show in their haemoglobin level after delivery; alternatively, they may have been unable to utilize iron during pregnancy but able to do so after delivery. These 12 patients were clinically well at all stages. Full haematological investigations were carried out in six of them, but no cause for their failure to respond was found.

It has been suggested that even if the fall in haemoglobin which occurs in pregnancy is not prevented by iron therapy the patients are none the worse clinically (Samuel, 1952). It is probable that this belief is widely held. In spite of repeated demonstrations that iron raises the haemoglobin in pregnancy, it is not administered routinely to pregnant women. It is, of course, difficult to prove that patients with haemoglobin levels above 90% are in better health than those with levels between 70 and 80%. One gains the impression that at the higher level they are more energetic and tire less easily; and there can be no doubt that they are in a better position to withstand haemorrhage or infection. Apart from the benefit to the patients, the confidence of both doctor and midwife, particularly in domiciliary practice, is greatly increased by the knowledge that the haemoglobin level is high at term.

Throughout this communication the figures quoted are averages, and averages are in some ways misleading. In this small series, 15 of the "responding" patients had initial haemoglobin levels of 80% or less. Some of these, if untreated, might have had terminal levels of 60% or less and would have been in a dangerous condition if not transfused during pregnancy. Considered on a national scale, it is probable that these dangerously low levels (sometimes but not always detected and treated by transfusion) could be avoided in the vast majority of cases by iron therapy.

It is customary to given iron to pregnant women who are "really" anaemic, the critical level at which treatment is considered necessary varying from one centre to another. When facilities for haemoglobin estimations are not readily available the presence or absence of "anaemia" is sometimes judged clinically. This is highly fallacious, as one of us (M. F.) proved some years ago by comparing the haemoglobin levels in pregnant women as judged clinically and estimated in the laboratory. Comparisons were made on 173 occasions and an error of 10% or more was observed on 87 of them. The limits of error were a clinical overestimation of 34% and an underestimation of 46%. In view of the findings in our series of patients, it would seem advisable to prescribe iron for all pregnant women and to see that it is really taken. If this is done it is doubtful whether routine haemoglobin estimations are necessary, though any patient with symptoms indicating anaemia should be fully investigated in case she is suffering from the rare macrocytic anaemia of pregnancy.

Conclusions

The administration of iron in pregnancy ensures a high level of haemoglobin at term in about 90% of cases.

It is suggested that giving iron as a routine to all pregnant women is a valuable and inexpensive preventive measure worthy of general application. The safety of domiciliary midwifery—which is questioned at times—would undoubtedly be increased by this means.

We are indebted to Dr. R. G. Macfarlane for helpful criticism, to Dr. Sheila Callender for the haematological investigation of "non-responders," to Dr. R. B. Fisher for statistical advice, and to Glaxo Laboratories and Roche Products Limited for generously supplying fersolate and ferro-redoxon respectively for this trial.

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RECURRING MENTAL CONFUSION AFTER PORTO-CAVAL ANASTOMOSIS

BY

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AND

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Alterations in the level of consciousness varying from light clouding to stupor and coma have been described after the operation of porto-caval anastomosis by McDermott and Adams (1954). Their patient had been so treated because of suspected carcinoma of the head of the pancreas, and "episodic stupor" could be induced readily by feeding with various nitrogenous substances. Earlier, Gabuzda *et al.* (1952) and Philips *et al.* (1952) noted that diets rich in nitrogen reduced many of their patients with cirrhosis of the liver to a state bordering on hepatic coma, and their findings are linked with the experimental work of Baló and Korpássy (1932), who produced "meat intoxication" in dogs with Eck fistulae. The mechanism is believed by Walshe (1951) and Riddell and McDermott (1954) to involve ammonia metabolism and the utilization of glutamic acid by the brain cells.

The electroencephalographic changes in developing hepatic coma have been reviewed by Adams and Foley (1953), who believe that constant although non-specific changes occur at first. These are paroxysmal, bilateral, and synchronous theta waves at 1½–3 c/s on a background of normal frequencies; gradually, with increasing mental confusion, the slow activity becomes dominant.

The following case is reported for its clinical interest and because the confusional episodes occurred spontaneously. They could also be induced by high-protein feeding and relieved by the reverse procedure.

Case Report

A Merchant Navy officer aged 52 was first seen on March 13, 1954. There had been excessive indulgence in spirits since 1923, but, apart from intermittent epigastric pain, no illnesses occurred until 1943, when he had jaundice. He recovered after some weeks, but in 1944 contracted syphilis, for which he was treated energetically with neoarsphenamine, the blood Wassermann reaction becoming negative. In 1952 there was a small haematemesis, and in February, 1953, a more severe one with melaena.

He was admitted to the Royal Victoria Hospital, Belfast, under the care of Dr. Robert Marshall, the chief physical findings being a firm palpable enlargement of the liver and spleen. On March 27, 1953, Professor H. Rodgers did a laparotomy. A cirrhotic liver was found, and a portal phlebogram showed gross intrahepatic distortion. A porto-caval shunt operation was performed. The post-operative period was marked by a low-grade pyrexia and slight jaundice, but on discharge on April 29 he was feeling fairly fit and had no symptoms or signs apart from the firm palpable liver, two fingerbreadths below the costal margin.

From that date until his readmission a year later, he had at least five attacks of "confusion," of which he had a hazy recollection. He readily admitted that most of the details had been furnished by his wife. The attacks described had a similar pattern, but varied a little in their effects. The first symptoms included "shakiness in the hands," noted especially when eating, writing, or dressing himself, and blurring of vision. He would feel "stupid" and unable to concentrate, and was difficult to waken in the morning. The most striking episode occurred in November, 1953. Late one evening, just before retiring, he wanted to pass water but could not find the lavatory. He wandered all over the house, and then eventually went to bed unrelieved. Some hours later he got up and renewed his search. This time his wife noticed his peculiar behaviour and showed him the way: but after relieving himself he found he did not know how to unlock the door. His wife eventually had to go outside and climb in through the window to let him out. The following morning he was wakened with difficulty and then proceeded to dress himself, but, in his own words: "I could not get my clothes on properly. They were either inside-out or upside-down." His wife watched, amazed at his performance and his persistence in trying to dress, but when she went to help him he resented interference, and nearly one and a half hours elapsed before he had his trousers on properly. In the other episodes he was noted to be querulous and unreasonable at times, and on one occasion he micturated on the floor of the sitting-room. The patient himself did not relate his attacks in any way to increased ingestion of food.

He was readmitted in March, 1954, to the neurological department, having been referred to us by Professor Rodgers. He was fully orientated and co-operative, and displayed no definite signs of impaired mental function on formal testing. The tendon reflexes were symmetrically increased, but the plantars were flexor. There was a fine rapid tremor of the outstretched hands. No other abnormal signs in the central nervous system were elicited. The blood pressure was 170/100 mm. Hg, and there was a precordial systolic murmur, but no diastolic murmur was heard. The breath at times had a peculiar odour, difficult to describe—like fresh meat or concentrated liquid extract of vitamin B. The liver was firmly enlarged to two fingerbreadths below the costal margin and was slightly tender. There was no evidence of ascites.

The results of recent chemical and radiological tests are compared in the Table with those of a year previously.

Investigations

	February and March, 1953 (Pre-operative)	May, 1954
Blood W.R.	Negative	Negative
Bromsulphthalein excretion	3% retention	17% retention
Plasma proteins	6·8 g.%; A/G ratio 1·8	5·8 g.%; A/G ratio 3
Thymol turbidity	4 units	1·0 unit
Serum bilirubin	0·6 mg. per 100 ml.	0·8 mg. per 100 ml.
Alkaline phosphatase	8 units K.A.	12 units K.A.
Urinary chromatogram	Slight excess in amino-aciduria of a general pattern	Slight excess in amino-aciduria of a general pattern
Blood group	AB, Rh-positive	
Haemoglobin	56%	94%
Colour index	1·0	1·0
White-cell count	7,200/c.mm. (normal differential)	6,500/cmm.
X-ray chest		No significant lesion
Barium swallow	Suggestion of oesophageal varices	No evidence of varices
Barium meal	Normal	Normal
Serum copper		228 μg. per 100 ml. (normal 99–111 μg.)
Urinary ,,		0-230 mg. in 24 hours
Lumbar puncture		Pressure, 90 mm. C.S.F.: cells, 1; protein, 20 mg. per 100 ml.; W.R. negative
Glucose-tolerance test		Lag storage curve
Insulin-sensitivity test		Some resistance to insulin

Methods of Investigation.—The patient was given a basic diet containing 70 g. of protein daily. Additional protein was given by mouth in the form of "casilan." Electroencephalograms were taken at regular intervals and the mental state was assessed by observing the behaviour and applying simple tests for his ability to concentrate (counting forwards and backwards), to register and recall (name and address), to calculate, and to grasp simple problems (Kohs blocks) (see Fig. 1).

On a diet containing 170 g. of protein, the E.E.G. showed excess slow activity, he was unable to concentrate well, and his performance with the Kohs blocks was impaired. Within

24 hours of giving 270 g. of protein daily, both the E.E.G. and the mental state became grossly abnormal, the behaviour corresponding to that of his condition previous to admission. Thus on one occasion he wandered around the ward looking for the bathroom, and was quite indignant when told that another patient's cubicle was not the lavatory. He was observed to have considerable difficulty in dressing himself, and he complained of blurring of vision and "shaking." The fetor of the breath was striking. The tremor of the hands became more coarse with flexion and extension movements at the wrist, giving the "flapping" appearance emphasized in most reports, and recently by Sherlock *et al.* (1954). It is of interest that it was more pronounced in the right hand. He was disorientated in place and time, and was unable to draw the points of the compass, in doing which at other times he was accurate.

Examination of the cerebrospinal fluid at this stage gave normal results, the blood-sugar values being also in the normal range. The injection intravenously of 50 ml. of 50% glucose had no effect. However, as the daily protein intake was reduced so both the mental state and the E.E.G. returned to normal. Two values of the blood ammonia were taken, using the technique described by Conway (1935), and were found to be significantly raised.

Discussion

Other possible explanations for the symptoms considered in this case were neurosyphilis and hypoglycaemia, but the blood and cerebrospinal fluid were quite normal and there was no alteration in the state of the reflexes or in the pupils. Insulin sensitivity was investigated and the effect on the blood sugar of physical exertion noted, but the results were against any association with hypoglycaemia. Further, there was the convincing manner in which the symptoms and abnormal electroencephalographic findings could be reproduced by a high-protein diet. If this is the explanation, it is somewhat surprising that such quantities of protein were necessary to produce them. The patient's wife had no doubt that he did not eat comparable amounts at home, where the same symptoms were first noted. However, when the protein intake was reduced the symptoms were reversible within 24 to 48 hours. It is possible that at home some added factor, such as alcohol or an intercurrent infection, combined to produce symptoms with a lower intake of protein, but we could not obtain any confirmation of this suggestion.

The normal pressure and the cellular and protein content of the cerebrospinal fluid at the time when confusion was maximal are in agreement with other workers (Adams and Foley, 1953). In spite of the clinical evidence of cirrhosis, except for the bromsulphthalein excretion liver-function tests were normal, so that it is likely that the presence of the shunt itself is significant in producing the disordered metabolism as suggested by Singh *et al.* (1954). The E.E.G. abnormality also proved reversible, the slow bilaterally synchronous waves giving way to a normal alpha rhythm (Fig. 2).

We would like to emphasize that we found the E.E.G. an extremely reliable and sensitive guide in predicting mental changes. Thus the most abnormal record preceded by 12 hours the development of severe confusion. The dressing dyspraxia was interesting. Experience with this case suggests that the symptom, although often a feature of parietal lobe disease (Critchley, 1953), is without localizing value and depends to some extent on a general lowering of the level of consciousness.

Summary

The case of a man aged 52 with cirrhosis of the liver is described. Following porto-caval anastomosis for portal hypertension, several episodes of mental confusion occurred which could be reproduced by high-protein feeding. Reversible E.E.G. changes were also seen giving way to a normal alpha rhythm. A high-protein diet is contraindicated in such patients.

Acknowledgments are due to Professor H. Rodgers for giving us the opportunity of investigating this patient. We thank Dr. J. H. D. Millar for the E.E.G. reports and Miss A. Coey, senior electroencephalographer, for technical assistance. We are also grateful for the advice Mr. D. Neill, of the biochemical department, gave us in planning tests and for the copper and ammonia estimations.

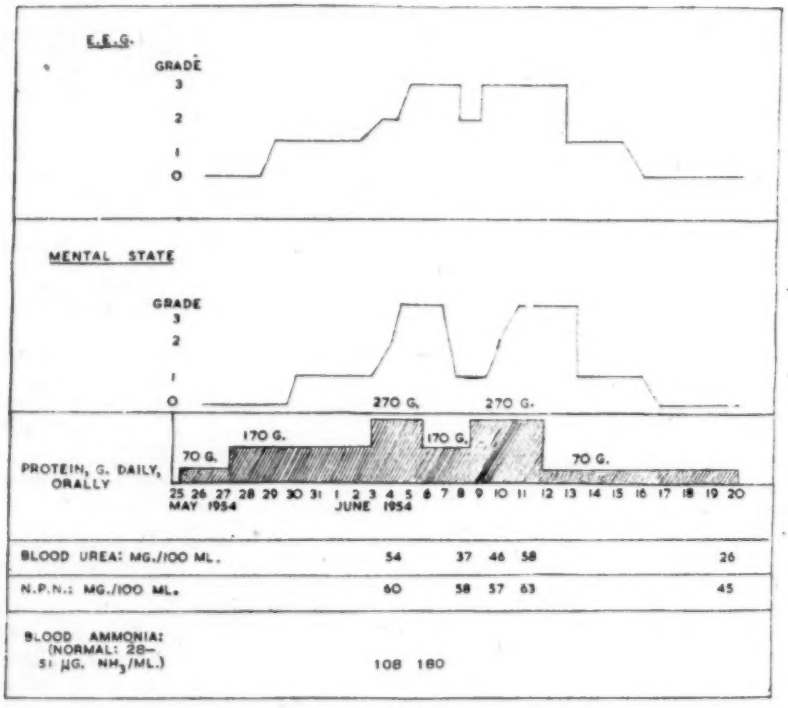

FIG. 1

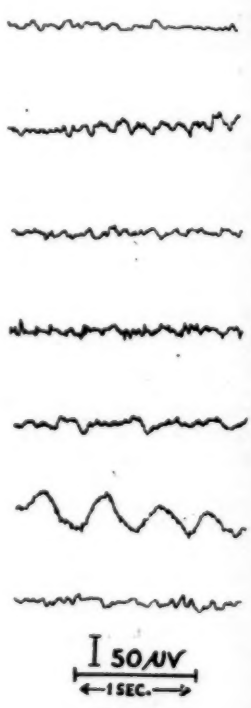

FIG. 2

FIG. 1.—Results of investigation. Normal electroencephalographic record before increased feeding: grade 3, 3 c/s waves, main activity; grade 2, moderate excess; grade 1, slight excess, slow activity; grade 0, normal. Mental state: grade 3, disorientated, dressing dyspraxia, etc.; grade 2, tremor, blurring of vision, drowsy; grade 1, impaired concentration; grade 0, normal.
FIG. 2.—E.E.G. recordings taken, from top to bottom, on May 27, 29, and 31, and June 2, 4, 11, and 17, 1954.

ADDENDUM

We have seen another case through the courtesy of Professor G. M. Bull in which dressing dyspraxia was a prominent feature.

Case Report.—A man aged 59 was first seen in September, 1953, with oedema of the legs, ascites, and hypertension (210/120). A continuous venous hum was heard in the epigastrium (Cruveilhier-Baumgarten syndrome). A biopsy of the liver showed multiple nodular hyperplasia. He was treated with a high-protein diet and kept well until August, 1954, when his doctor reported: "Yesterday the patient became rather confused, and attempts to dress himself were unsuccessful." He was also reported to have melaena. On admission there was jaundice, and he was apathetic and disorientated. On examination there was enlargement of the liver and spleen, and ascites, and the venous hum was very marked. With treatment by low-protein diet he made a good recovery.

An annotation in the *British Medical Journal* (1954) refers to the dual role of liver damage and the effects of a porto-caval shunt in producing mental symptoms. It seems to us, however, that a third factor, not mentioned by the annotator, is important. In the first case described, alcohol and intercurrent infection, and in the second, gastro-intestinal bleeding, may have played a part in precipitating the confusional episodes. One of us (Allison, 1952) has emphasized how often anoxia, dehydration, alkalaemia, the injudicious use of drugs, and electrolytic imbalance lead to psychiatric disturbances in later life. In both our cases the possible ancillary action of some such factor cannot be excluded.

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MUSCULAR DYSTROPHY OCCURRING IN IDENTICAL TWINS

BY

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Since the second half of the nineteenth century muscular dystrophy has been recognized as a hereditary disorder (Gowers, 1879; Erb, 1891) although there has been disagreement about the way it is inherited. Much difficulty was experienced in the classification and genetics of the many varieties described. Recently further attempts were made to introduce simpler classifications, but, owing to the variability of expression of the defective gene and the similarity of the genetic types, difficulties remain.

After studying 1,228 cases from the literature and 113 case records from the National Hospital, Queen Square, Bell (1943) divided the dystrophies into three clinical groups: group A, the pseudo-hypertrophic form characterized by the enlargement of certain muscles, wasting of others, and progressive weakness in all affected muscles; group B, cases with wasting and weakness of the affected muscles, no history of enlargement, and no affection of the facial muscles; group C, all cases in which the facial muscles were affected. She considered that there were three genetic groups—recessive, dominant, and sex-linked—and that the same gene could produce any of the three clinical types. This theory was supported by Boyes *et al.* (1950), who studied the history of an English and Canadian family in which both group A and group C occurred, the family distribution indicating a simple dominant type of inheritance.

More recently Tyler and Stephens (1950, 1951) suggested making only two groups: the childhood and the facio-scapulo-humeral groups. For the first type they preferred the term "progressive muscular dystrophy of childhood" to the more usual one of "pseudo-hypertrophic muscular dystrophy," as pseudo-hypertrophy may sometimes be absent in this group and present in the second one. This illness runs a steadily progressive downhill course, terminating fatally in adolescence or young adult life. It occurs only in males and is transmitted by females, the gene being a sex-linked recessive. The facio-scapulo-humeral type is inherited as a simple dominant affecting both sexes and half the offspring with a wide variability of expression and penetration. It starts usually in young adult life and runs a very variable course. Tyler and Stephens studied a large family in Utah founded by an affected emigrant born in 1775. In six generations there have been 1,249 descendants, of whom 159 have been affected with dystrophy of the second type. A similar classification was favoured by Ramsey and McCarroll (1952).

After studying 71 cases at Massachusetts General Hospital, Brown (1951) was unable to make a rigid classification but considered that the cases fell into three main groups: group 1, cases with pseudo-hypertrophy; group 2, cases with generalized muscular atrophy starting in the thighs; and group 3, cases with generalized muscular atrophy starting in the scapulo-humeral muscles.

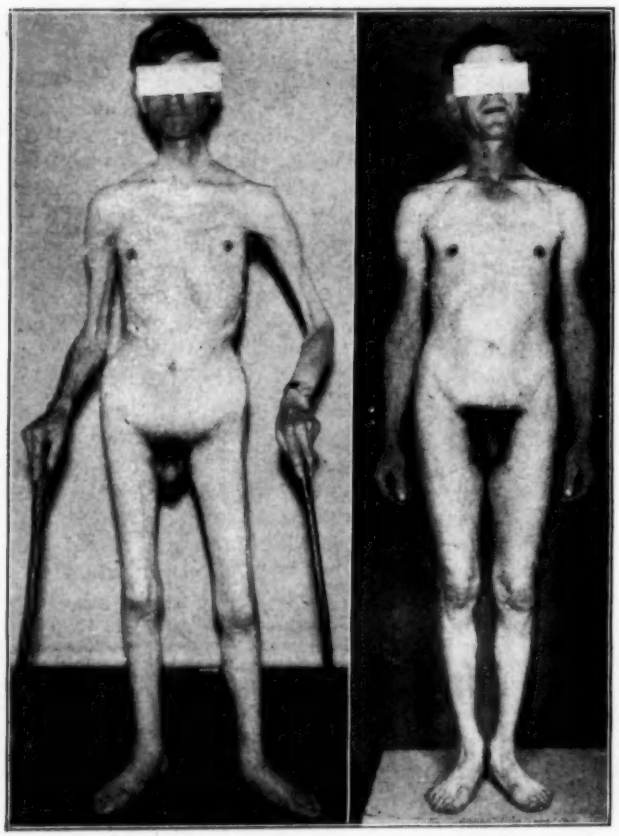
Stevenson (1953) studied all the known cases of muscular dystrophy in Northern Ireland together with their families. There were 72 cases in 51 families. He concluded that there are only two groups: (*a*) the pseudo-hypertrophic variety occurring in boys and transmitted as a sex-linked recessive disease. For this he suggested the clumsy but more accurate title, "Duchenne type rapidly progressive muscular dystrophy of young boys"; (*b*) the second group consists of all the other types which he believed to be variants of the same condition determined by single autosomal recessive gene inheritance. For this group he suggested the term "autosomal limb-girdle muscular dystrophy."

The occurrence of a disease in twins is helpful in studying its heredity. Few twins, however, have been affected with muscular dystrophy, and so far there has been no report of the variety without hypertrophy occurring in identical twins. Stephens and Tyler (1951) described male identical twins who had the pseudo-hypertrophic form. The disease ran an identical course in each, being first recognized at the age of 6 years, causing complete incapacity at 11 years, and death, within a few months of each other, at the age of 25. No other member of this family was affected. The occurrence of progressive muscular dystrophy (without hypertrophy) in a male twin but not in the corresponding female has been reported by Milhorat and Wolff (1943) and Karnosh and LaTona (1947).

The cases reported here occurred in identical twin males who had muscular dystrophy of the autosomal limb-girdle type ; one was severely affected, but the other only mildly so.

Case 1

An unmarried man aged 45 was sent to hospital to obtain an invalid chair. At the age of 18 he had noticed weakness of the legs, which was worse proximally. The weakness increased gradually during the next 13 years until after an attack of influenza at the age of 31 it became much worse and affected the shoulder muscles. Progressive weakness made him retire at the age of 38 from his work as a farm labourer with some blacksmith's duties. Deterioration continued slowly until a second attack of influenza at the age of 48, when again the weakness and atrophy increased rapidly, particularly in the legs. He has had no other illnesses.



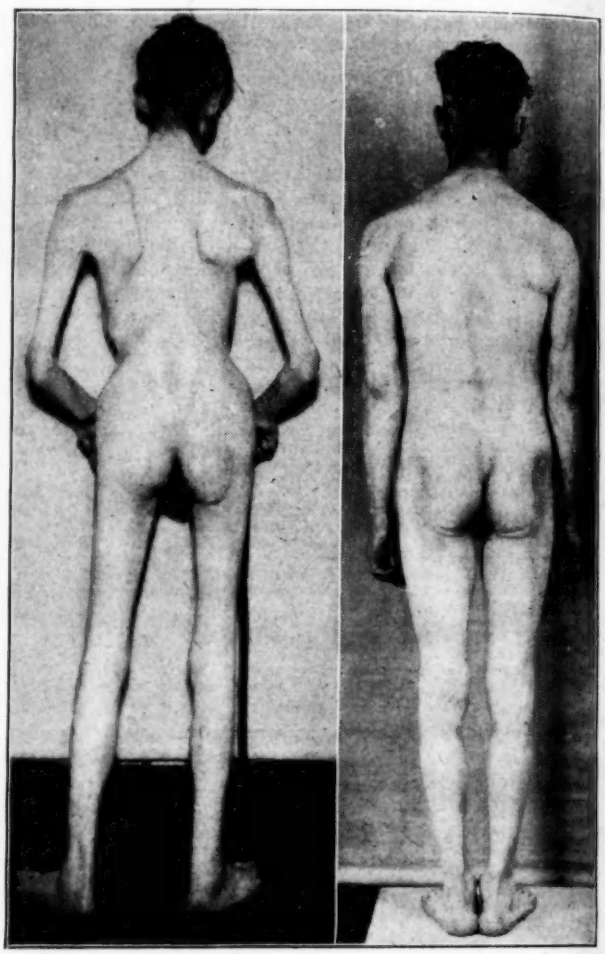
Case 1. Case 2.

On examination there was postural oedema of the feet but no other abnormality outside the muscular system. The gait was waddling, with marked lumbar lordosis. The buccinator muscles were weak but the other facial muscles were normal. The sterno-mastoid muscles were severely affected, being very weak and wasted. There was marked wasting of the shoulder-girdle muscles with winging of the scapulae. The deltoids were moderately weak and atrophied, as were the biceps and triceps, but the muscles of the forearms and hands were not so severely affected. The intercostal and spinal muscles were weakened and wasted. There was severe weakness of all the muscles acting on the hip-joint, so that he was unable to raise his legs against gravity. The severe weakness and wasting of the legs was more marked proximally. No fasciculation was visible. Tendon jerks were diminished, commensurate with the muscular weakness. Plantar responses were flexor. There was no sensory loss. He was confined to the house, being unable to walk more than a few yards, and this only with the aid of sticks. He could not get up from a sitting position without help, and once up could stand unsupported for only a few minutes.

Case 2

The twin brother, married but without children, was not aware that he was affected. He was able to do general farm duties without difficulty.

On examination no abnormality outside the muscular system was found. There was slight hypertrophy of the right deltoid. The legs were wasted, particularly the quadriceps, sartorius, and calf muscles. No demonstrable weakness was seen. No fasciculation was visible. Knee- and ankle-jerks were slightly diminished. There was no sensory loss.



Case 1. Case 2.

The twins were not weighed at birth, but were not full-term. The younger twin (Case 1) was born ten minutes after the other, there being one afterbirth, which came after the second twin. The parents observed that the younger twin was always a little slower than the elder, but there was no other difference between them as children. They were identical physically and were mistaken for each other even until recently. No other member of the family is known to be or to have been affected.

Discussion

In the younger, more seriously affected, twin the disorder started first in the proximal muscles of the legs. It has affected the facial muscles and has not produced any

hypertrophy. Thus the case falls into Bell's group C. In the elder twin the right deltoid is larger than the left, but this may well be work hypertrophy. His legs are the parts most affected, the facial muscles not at all. Thus his disorder falls into Bell's group B. Both cases fall into Brown's group 2, Tyler and Stephens's group 2, and Stevenson's "autosomal" limb-girdle muscular dystrophy group.

The physical characteristics of the twins were carefully examined in an attempt to establish that they were identical. There was a striking physical resemblance in spite of the marked wasting of the younger twin. The colours of their hair and eyes were the same; their height differed by only ½ in. (1.3 cm.), whilst their biparietal, fronto-occipital, and bizygomatic diameters differed by no more than ¼ in. (6 mm.).

Their main blood groups were the same: ABO: A_1; Rh: CDe/cde; MN: M. The subgroups, done by the Blood Group Reference Laboratory, were the same:

	S	P	Lu^a	Kell	Le^a	Le^b	Fy^a
Case 1 ...	+	+	−	−	−	+	+
Case 2 ...	+	+	−	−	−	+	+

Although the fingerprints of identical twins are not the same, the fingerprints of these twins are of interest. All the impressions of the younger twin were of the type known as "ulnar loop" with the exception of the right forefinger, which was a radial loop, whereas the impressions of the elder twin were all ulnar loops except that of the left forefinger, which was the same pattern as that of the right forefinger of the younger twin—that is, radial.

These findings, although not conclusive, support the opinion of the family that the twins are identical.

It is noteworthy that the younger twin is severely incapacitated, whereas the elder is so mildly affected that he does not realize that he has the disorder. This raises the question of whether there is some environmental factor which determines the severity of the disease.

Boyes *et al.* (1950) found that in several of their cases the onset of the disease was associated with a specific environmental stress, and that a period of unusual physical strain precipitated the onset of the disease in the muscles under stress. Thus in one case the disease started in the shoulder of a woman after working long hours as a waitress carrying trays, and later affected her legs in pregnancy.

In the present cases no such explanation could be found. Both were brought up on the same farm and have lived in the same area since, the younger twin remaining at home and the elder at the age of 17 moving to the farm of an uncle only ten miles away. Their modes of life, nutrition, and work on the two farms were similar.

The two illnesses described by the younger twin as influenza caused marked deterioration on each occasion. It is possible that these illnesses were caused by a particular strain of influenza virus or some unusual type of virus which did not affect the other twin. It is more probable, however, that they were ordinary influenzal attacks, that the other twin has had similar attacks, and that some other unidentified factor has been responsible for the marked difference between the two.

Summary

Muscular dystrophy is reported as occurring in identical male twins now aged 45; in one the disease is severe and incapacitating, but in the other it is so mild that he is unaware that he is affected. No explanation can be given for this difference.

I wish to thank Dr. A. P. Dick for permission to publish these cases and for his help in the preparation of the report; Dr. Helen Dimsdale for her criticisms; Dr. C. B. V. Walker, of the Blood Transfusion Service, Cambridge, and Dr. D. M. Parkin, of the Blood Reference Laboratory, for their opinions in the blood grouping; Mr. P. Graham for the photographs; and the superintendent of the Huntingdonshire County Constabulary for the fingerprints.

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ESSENTIAL PENTOSURIA*

BY

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Essential, or idiopathic, pentosuria is a rare condition which has been included by Garrod (1923) among the inborn errors of metabolism. Its occurrence was first described by Salkowski and Jastrowitz in 1892, but since then only about 200 cases have been recorded in the literature, and only one clinical report dealing with the condition has been published in this country—namely, that of Cammidge and Howard, which appeared in 1920 and described seven cases. The early case reports have been reviewed by Garrod (1923) and Margolis (1929a), and, more recently, Bock (1944) has summarized the features of the condition in a review of the benign meliturias. Since 1944 case reports have been added by Bloomberg *et al.* (1946), Caven (1947), and Barnes and Bloomberg (1953).

The clinical importance of pentosuria depends on the fact that it may be confused with diabetes mellitus. Nowadays, however, when chemical confirmation of a diagnosis of mild diabetes is almost a universal practice, it is more likely to be misdiagnosed as renal glycosuria.

The identification of urinary reducing substances has been greatly facilitated by the introduction of paper chromatography. In the department of clinical pathology at University College Hospital we have been applying this method to identify the reducing substance excreted in cases which appear to have a low renal threshold for glucose. In the course of 4½ years two cases of essential pentosuria have been encountered. These two cases are described here and existing knowledge of the condition is reviewed.

The following methods were used: (1) Qualitative Benedict tests (Flynn *et al.*, 1953). (2) Bial's test (Lasker, 1950). (3) Osazones (Enklewitz and Lasker, 1935a). (4) Blood sugar (Hagedorn and Jensen, 1923). (5) Urine nitrogen (micro-Kjeldahl). (6) Urine xylulose (Lasker and Enklewitz, 1933), using the factor of Greenwald (1930a) for the calculation. (7) Chromatography (Horrocks and Manning, 1949), using a 3:2:1.5 *n*-butanol-pyridine-water solvent (Hough *et al.*, 1950) as well as the 4:5:1 *n*-butanol–acetic-acid–water mixture of Partridge and Westall (1948). The paraphenylenediamine reagent of Flynn *et al.* (1953) was used for showing up the sugar spots on the paper chromatograms.

*Based on a communication read at a meeting of the British Diabetic Association on July 17, 1954.

Case 1

A married Hungarian Jewess aged 34 was admitted to University College Hospital under the care of Dr. J. F. Stokes in May, 1950, suffering from infective hepatitis. During her stay in hospital it was noted that her urine gave a yellowish-green reduction of Benedict's reagent.

History of "Glycosuria."—Sugar was first discovered in the urine in October, 1947, when the patient was in University College Hospital under Dr. F. M. R. Walshe, with poliomyelitis. So far as she was aware this was the first time her urine had been tested. She was referred to the diabetic clinic, but failed to attend. She had no symptoms suggestive of diabetes at any time apart from two boils in October, 1949. She had gained 2–3 st. (12.7–19 kg.) in weight in the last three years. Glycosuria had been noted more than once by the several doctors she had consulted in the previous year, but she was told that her blood sugar was normal and that she had renal glycosuria.

There was no family history of diabetes, though the patient recalled that one of her three siblings had once been thought to have sugar in the urine.

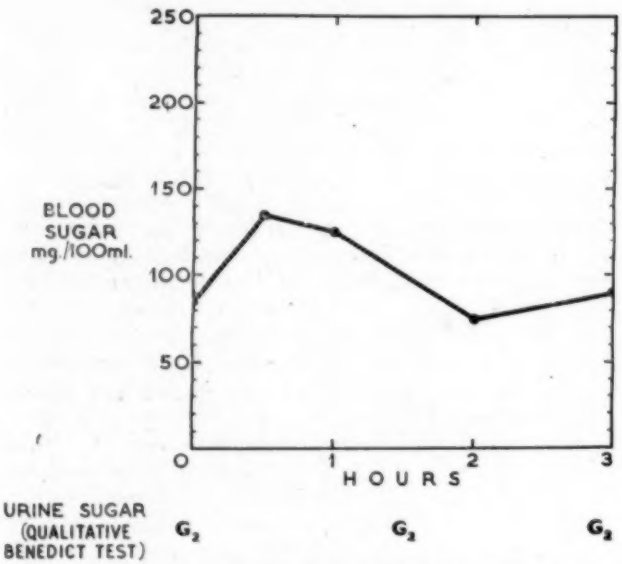

FIG. 1.—Blood-sugar curve in Case 1 after 50 g. oral glucose. G_2=yellowish-green reduction.

Investigation of "Glycosuria"

The urine was tested repeatedly over a six-day period. Reduction of Benedict's reagent was found to occur with all specimens, regardless of the time of day; most gave a yellowish-green reduction. Rothera's test was consistently negative.

A glucose-tolerance test was performed, the result being shown in Fig. 1. This shows a normal blood-sugar curve, but sugar is present in all three specimens of urine, the concentration being the same in each.

Paper chromatography of the urine disclosed the presence of a small amount of glucose and glucuronate and a large amount of another substance which we had not previously encountered. This unknown substance moved relatively fast on the chromatogram and was recognized, by the reddish colour produced on spraying with paraphenylenediamine, as being a pentose. The R_F value of this sugar was greater than that of xylose or arabinose, however, and was nearest to that of rhamnose. Subsequently we realized that the sugar must be xylulose (also known as xyloketose), and were able to confirm this by showing that it gave the typical chemical reactions, and had an identical R_F value to that of a synthetic xylulose solution prepared from xylose according to the method of Schmidt and Treiber (1933).

Chemical studies showed that the urine gave a positive Lasker–Enklewitz test (see below), and a positive Bial test. The reducing property of the urine was destroyed by treatment with dilute hydrogen peroxide solution (Enklewitz, 1936), and by heating with strong acid (Enklewitz and Lasker, 1933), but treatment with bromide did not affect the results of reduction tests (Greenwald, 1930a). An osazone was prepared which showed the typical properties of L-xylosazone (Greenwald, 1930a, 1930b; Barnes and Bloomberg, 1953). Direct examination of the urine in the polarimeter did not disclose any optical activity.

The concentration of xylulose was estimated in a random afternoon specimen of urine and was shown to be 0.5 g. per 100 ml. The concentration of other reducing substances present was 0.2 g. per 100 ml. (when expressed as xylulose).

Case 2

A German Jewess aged 55 first attended Professor M. L. Rosenheim's out-patient clinic at University College Hospital in February, 1951, having been referred by her doctor on account of hypertension. Diabetes was said to have been present for 30 years. On examination the only abnormal findings were a blood pressure of 225/130 and a bluish-green reduction of Benedict's reagent on testing the urine. No ketones were present. A diagnosis of benign essential hypertension was made.

History of "Glycosuria."—In 1919, when the patient was aged 24, her urine was tested for the first time. She had been feeling unwell immediately following her father's death, and while in Austria consulted a chemist, who found sugar and acetone in her urine. She had lost much weight, and her cousin, a doctor, diagnosed diabetes. She was put on a strict diet in a clinic at Wiesbaden, and subsequently attended there each year for 12 years. In 1920 she was said to have had a coma. In 1923 she was given two injections of insulin, with severe reactions. In 1933 she gave up going to Wiesbaden and ceased to worry about her diet, as she found she kept well without it. She returned to it, however, before visits to her doctor. In 1936 insulin was tried again and was followed by fairly typical hypoglycaemic attacks. In 1941 she was in hospital in this country on account of pyrexia of unknown origin. Routine testing of the urine revealed sugar, and she was again advised to take insulin, but refused to do so.

It is also noteworthy that she underwent appendicectomy in 1924, left radical mastectomy in 1933, hysterectomy in 1943, and a further gynaecological operation in 1946, all without complications.

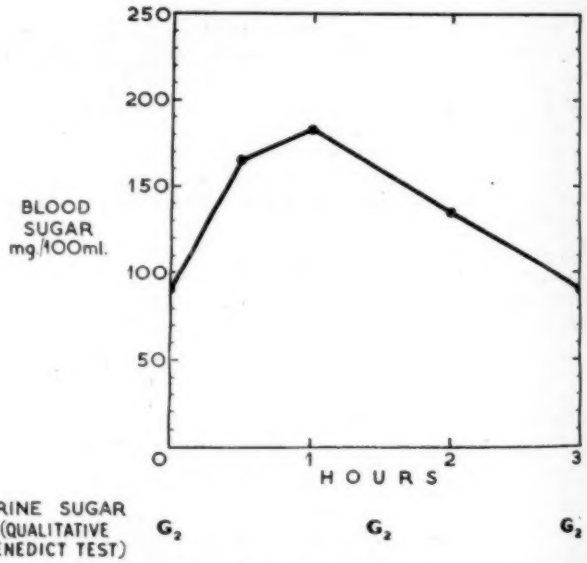

FIG. 2.—Blood-sugar curve in Case 2 after 50 g. oral glucose. G_2=yellowish-green reduction.

The family history revealed that her father and her maternal grandfather had been known to have small amounts of sugar in the urine, but none of her five sisters was known to be so affected.

Investigation of "Glycosuria"

A glucose-tolerance test was performed, and the result is shown in Fig. 2. This shows a blood-sugar curve which is just within normal limits, but sugar is present in all three specimens of urine, the concentration being the same in all and unrelated, therefore, to the height of the blood sugar.

The urine-reducing substance was shown by paper chromatography to be a pentose and was subsequently identified,

FIG. 3.—Paper chromatogram of urine sugar from Case 2 with appropriate markers.

as in Case 1, as xylulose. A chromatogram of a later specimen of this patient's urine, with appropriate markers, is reproduced in Fig. 3, and shows the presence of glucuronic acid and xylulose. The large quantity of glucuronic acid in this specimen was due to prior administration of glucurone.

Further tests, carried out in June, 1951, when the patient was admitted to the wards, showed that the condition was in every way typical of essential pentosuria. The results (Figs. 4 and 5) show: (*a*) that the daily excretion of xylulose is constant at about 3.5 g. a day when no drug is being given, regardless of minor changes in the diet; (*b*) that xylulose excretion is not affected by feeding fructose; (*c*) that xylulose excretion is increased by administration of glucurone and amidopyrine; (*d*) that xylulose excretion is not related to nitrogen output; (*e*) that xylulose excretion is not related to urine volume; (*f*) that the rate of xylulose excretion rises more rapidly after glucurone than amidopyrine; and (*g*) that there is a direct relationship between glucuronate and xylulose excretion.

We were also able to demonstrate xylulose in the plasma by heavily loading protein-free filtrate on to paper chromatograms. It was just detectable in the fasting state, but the concentration was increased following administration of glucurone.

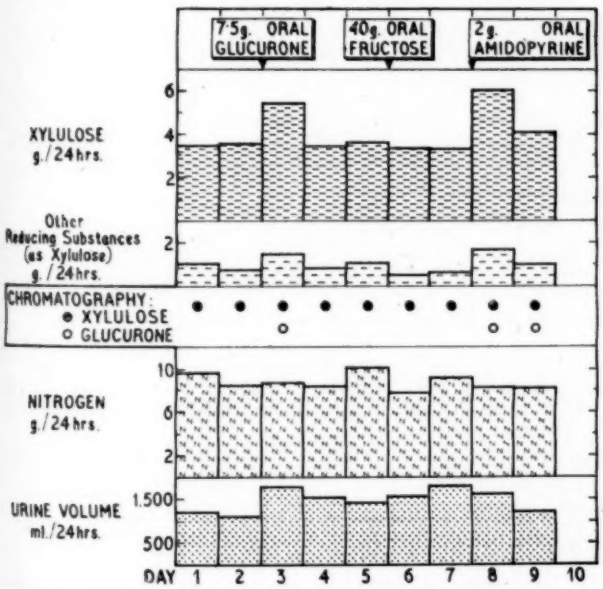

FIG. 4.—Urine findings during metabolic investigations in Case 2.

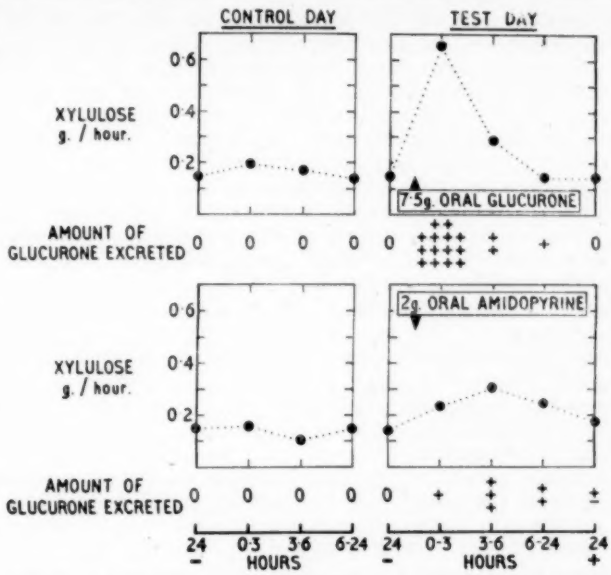

FIG. 5.—Correlation between urinary excretion of xylulose and glucuronate in Case 2. (Glucuronate excretion assessed from size and intensity of spot on chromatogram.)

Urine specimens were obtained from the one relative resident in this country—a sister—and the first specimen reduced Benedict's reagent and showed xylose on chromatography. This startling finding must be attributed to fruit-eating, for subsequent specimens were sugar-free.

Discussion

Types of Pentosuria

These two cases are typical of essential pentosuria, which is characterized by the constant excretion of small amounts of L-xylulose. Other forms of pentosuria from which this condition has to be distinguished are alimentary pentosuria, in which arabinose or xylose is found in the urine after ingestion of a large amount of fruit or fruit product, and possibly also ribosuria, which has recently been claimed to accompany some cases of muscular dystrophy (Minot *et al.*, 1949; Orr and Minot, 1952).

Features of Essential Pentosuria

The incidence of essential pentosuria has been estimated from insurance records to be 1 in 50,000 (Larson *et al.*, 1937). It is found almost exclusively in people of Jewish lineage, but proved cases have been recorded in non-Hebrews (Barnes and Bloomberg, 1953). There is a distinct familial tendency, and the studies of Lasker *et al.* (1936) indicate that the disorder is inherited as a simple recessive. The condition has been found more often in males, but, as pointed out by Bock (1944), this may merely reflect the fact that more males than females apply for life assurance. It has been discovered at all ages, and persists throughout life. As yet no case has been proved to be present from birth.

The condition appears to be harmless to health. Margolis (1929a) noted that a high proportion of these patients suffered from headaches and were psychoneurotic; such symptoms, however, may have resulted from the patients worrying unduly about their so-called diabetes. In all cases reported by Cammidge and Howard (1920) excess urobilin and amino-acid nitrogen were found in the urine. This finding has not been confirmed by others and there was no amino-aciduria in either of the cases reported here. Excess urobilin was not found in the urine of Case 2 at any time.

The salient feature of essential pentosuria is the continuous excretion in the urine of small amounts of

L-xylulose. Usually 2–5 g. is excreted per day, the amount apparently varying with body weight (Enklewitz and Lasker, 1933); the concentration is always less than 1%. In the early literature arabinose was reported to be the sugar excreted, but later workers have agreed with Levene and La Forge (1914) that L-xylulose is the sugar present. Many cases reported as arabinosuria were in all probability cases of xylulosuria; indeed, two such cases have been proved to be so (Lasker, 1950). Wolfson *et al.* (1949) and Barnes and Bloomberg (1953) have shown by paper chromatography that pentosurics may excrete traces of xylose and other sugars in addition to xylulose.

For a given patient the amount of xylulose excreted is constant from day to day regardless of diet (Enklewitz and Lasker, 1935a). Feeding hexoses or pentoses is without effect (Cohen, 1910; Cammidge and Howard, 1920; Englewitz and Lasker, 1933; Bloomberg *et al.*, 1946), but fasting for 24 hours has been shown to halve the excretion (Enklewitz and Lasker, 1933). It has been claimed that the xylulose excreted paralleled the purine and protein content of the diet (Janeway, 1906; Cammidge and Howard, 1920), but Margolis (1929b) was unable to confirm this, and our results in Case 2 do not show an obvious relationship between nitrogen and xylulose excretion. Exercise and administration of thyroid and insulin are without effect on xylulose excretion (Rabinowitch, 1925; Enklewitz and Lasker, 1933), but feeding glucuronic acid or drugs which are excreted as glucuronates—such as amidopyrine and codeine—results in increased excretion (Margolis, 1929a, 1929b; Lasker and Enklewitz, 1933; Enklewitz and Lasker, 1935a), as demonstrated in Case 2.

Metabolic Defect in Essential Pentosuria

Enklewitz and Lasker (1935a) seem to have established that glucuronic acid is the precursor of L-xylulose in pentosurics. Thus feeding them glucuronic acid or drugs excreted as glucuronates leads to increased excretion of xylulose, but feeding conjugated glucuronate is without effect. Moreover, there appears to be a direct relation between the amount of glucuronic acid administered or produced in the body and the extra amount of xylulose excreted. Our results in Case 2 seem to bear this out. It is odd that feeding drugs which are excreted as glucuronates should lead to increased xylulose excretion; presumably they stimulate the formation of more glucuronic acid than is required for their conjugation.

As feeding glucuronic acid to normals does not lead to pentose excretion, the suggestion has been made that pentosuric patients have an abnormal enzyme system which decarboxylates glucuronic acid to yield xylulose (Everett, 1946). There is evidence, however, that L-xylulose may be a normal intermediary metabolite rather than an abnormal one. Thus L-xylulose appears to be metabolized by dogs (Greenwald, 1931; Larson *et al.*, 1939), and in a normal man, after oral administration of 5 g., none could be recovered in the urine in 24 hours (Enklewitz and Lasker, 1933). If L-xylulose is a normal metabolite in man then essential pentosuria could result from a block in the further metabolism of xylulose, for when 5 g. of L-xylulose was fed to a pentosuric an extra 0.5 g. was recoverable in the urine in the next 24 hours (Enklewitz and Lasker, 1933).

The nature of the error in essential pentosuria would appear, then, to be a partial or complete block in the metabolism of xylulose—one of the normal derivatives of glucuronic acid metabolism. A possible alternative explanation is that there is an abnormally large production of xylulose which overwhelms the mechanism that normally disposes of this sugar.

Diagnosis of Essential Pentosuria

Diagnosis depends on (*a*) discovering a constant melituria; (*b*) excluding diabetes by demonstration of normal glucose tolerance; and (*c*) identifying xylulose in the urine. Usually diagnosis is straightforward, but cases have been recorded with a coexistent diabetes (Edelman and Reiner, 1943), with diabetic symptoms (Enklewitz and Lasker, 1935b; Peterman, 1945), and where a reduction by the urine was not found in all specimens (Derivaux, 1943). In the case reported by Peterman the urine sugar was not proved to be xylulose.

Regarding tests for xylulose in the urine, that of Lasker and Enklewitz (1933) is an ideal screening test, as it can be readily performed by the clinician. It is carried out by adding 1 ml. of urine to 5 ml. of Benedict's qualitative reagent, mixing, and placing the test-tube in a water-bath at 55° C. for 10 minutes; if a water-bath is not available the mixture is left at room temperature for 3 or, preferably, 24 hours. The appearance of a yellow precipitate under these conditions is very suggestive of xylulose. Fructose, ascorbic acid, and glucose in high concentration may cause false positives, so confirmation is essential (Lasker and Enklewitz, 1933; Enklewitz, 1936; Barnes and Bloomberg, 1953).

For final identification of xylulose in the urine, paper chromatography provides the most satisfactory test, and is simpler than preparation and purification of osazones for melting-point and nitrogen determinations. With the use

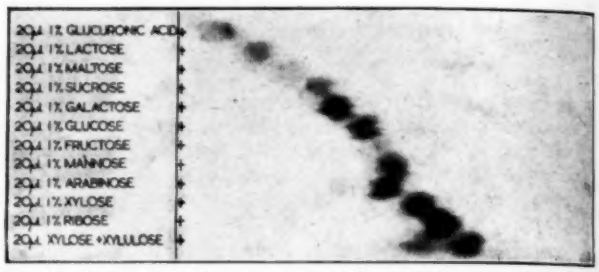

FIG. 6.—Separation of sugars by one-dimensional paper chromatography using 3:2:1.5 *n*-butanol-pyridine-water solvent.

of a butanol-pyridine-water solvent, and a spray reagent which distinguishes pentoses from hexoses, it is possible to identify all the urinary sugars on a one-dimensional chromatogram as shown in Fig. 6. It is likely that with the help of paper chromatography many more cases of essential pentosuria will be discovered.

Summary

Two unrelated cases of essential pentosuria are described; one masqueraded as diabetes mellitus, the other as renal glycosuria.

Results of metabolic investigations in one case are presented.

The features of the condition are reviewed and the nature of the metabolic defect is discussed.

The simple Lasker–Enklewitz test for detecting xylulose in the urine is described, and attention is drawn to the value of paper chromatography for final identification of the sugar.

I wish to thank Professor M. L. Rosenheim and Dr. J. F. Stokes for permission to publish these cases and for helpful criticism; Mr. A. J. Cummings for valuable technical assistance; Mr. V. K. Asta for the diagrams; Mr. A. Bligh for the photographs; and Dr. Ann Warrick for help with the manuscript.

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TRUE HERMAPHRODITISM

BY

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An individual who has both ovarian and testicular tissue is a true hermaphrodite. Proof of the presence of both types of gonad in the same individual is histological, as the secondary sex characters may be affected by other factors, such as overactivity of the adrenal cortex.

Adopting these criteria, an examination of the literature has disclosed 59 unequivocal cases of true hermaphroditism, to which two further cases are added below. The further progress of the case originally recorded by Broster *et al.* (1938) is also noted.

Case 1

J. O., the third child of healthy parents of English extraction, was first seen at the age of 16 months, having been brought for determination of the sex. No family history of any endocrine disease or congenital abnormality was forthcoming, except for talipes in the second child. The mother had suffered no illness during the pregnancy.

On examination the child appeared healthy and apparently normal except for the genitalia, which showed the following abnormalities. The phallus, about 3 cm. long, curved downwards and had a hooded prepuce. About 3 cm. behind the phallus lay an orifice into which opened the urethra and a short recess. This recess admitted a probe for 2.5 cm. and presumably represented the lower part of the vagina. The labio-scrotal folds were rugose and contained no testes or hernial sacs.

Investigations.—Urinary 17-ketosteroids, 0.3 mg. a day (this is at the lower limit of assay, and indicates only that the 17-ketosteroid excretion was not increased). *X*-ray examination of the pituitary fossa showed no abnormality. The epiphysial bone age was 2–3 years—that is, about one year more than the actual age.

Operation.—Mr. L. R. Broster performed a laparotomy on July 17, 1953. A small (4 cm.) uterus was observed, from which ran two Fallopian tubes, terminating in fimbriated ends. In the usual position of the right ovary lay a structure about 2 cm. long, resembling a testis, a portion of which was removed for microscopical examination. No epididymis or other Wolffian elements could be found on either side. The adrenal glands felt normal in size and consistency. Samples of skin were taken from both sides of the abdomen for examination of the somatic nuclei by the method described by Moore *et al.* (1953). Dr. W. E. Evans reported that the whole of the piece of tissue (8 by 3 mm.) from the right gonad consisted of immature testicular tissue, with seminiferous tubules separated by a loose, clear-celled stroma. Interstitial cells were not identified. A narrow fibrous capsule lay along one edge of the biopsy. The specimen, about 3 by 3 mm., from the left gonad consisted of a strip of young ovarian tissue beneath which was loose fibrous tissue. No ovarian "germinal" epithelium was found on the surface. Several ova were present, each surrounded by rather flattened cells with deeply stained nuclei, apparently derived from the ovarian stroma.

Skin Biopsies.—Professor M. L. Barr reported that a chromatin mass was present in less than 10% of epidermal nuclei. It has been observed (Moore *et al.*, 1953) that, in sections of tissue taken from a normal female, more than 80% of the nuclei seen contain a speck of chromatin on the periphery of the nucleus. In normal males such a mass is seen in less than 10% of nuclei in tissue sections. This observation is in accordance with the difference between the female sex chromosome pattern (XX) and the male pattern (XY). The nuclear picture in this case therefore conforms to the male type.

Case 2

P. F. was first seen in July, 1940, at the age of 20 months. The child had been brought up as a girl, but was already rougher and more masculine in behaviour than the elder sister, who was a normal girl. The patient was a muscular child with a deep voice and of normal intelligence. The phallus was about the normal size for a male of that age, but the urethra terminated at its base. No gonads could be felt in the scrotum, which was split, and a small uterus was palpated rectally.

Investigations.—Urinary 17-ketosteroid excretion, 0.3 mg. a day. Perirenal insufflation gave no evidence of adrenal enlargement.

Operation.—Laparotomy was performed on September 1, 1940, by Mr. L. R. Broster. A small infantile uterus with fimbriated Fallopian tubes was found. Two gonads lay in the position of the ovaries. The left gonad was the size of a pea and the right gonad was slightly larger. No epididymis or vas deferens was seen on either side. Both gonads were removed for microscopical examination.

Professor H. W. C. Vines reported that the left gonad consisted of ovarian tissue and the right gonad of fibrotic testicular tissue.

The child was clearly more male than female in its behaviour, and was therefore brought up as a boy. From the age of 4 years a series of operations were performed to correct the hypospadias. Injections and local inunction of testosterone from the age of 6 years have produced some increase in the size of the penis, which was, however, still smaller than normal when he was last seen in 1951 at the age of 13. He was then psychologically male, but rather shy, tending to cling to his mother.

Unfortunately, it has not proved possible to get in touch with the patient in order to obtain a sample of skin for nuclear examination.

Case 3

B. T. (Broster *et al.*, 1938) was regarded as a female at birth. At the age of 3 years, however, the child's social and legal sex was changed to male. Two years later hair began to grow on the face, legs, and pubis, and the voice cracked. When seen at the age of 9 years the child had a small penis with complete hypospadias and a split scrotum containing no testes. He was psychologically male. At laparotomy on November 30, 1936, at the age of 9, an infantile uterus with tubes was present. The gonads, which were in the position normally occupied by the ovaries, were shown by biopsy to be both ovotestes.

The patient's hypospadias was successfully repaired at the age of 14, and since then injections and implants of testosterone have been given to encourage penile growth.

When last seen, in January, 1954, he had the appearance of a normal adult male except for a small penis and no

testes in the scrotum. The nipples and areolae have a brown pigmentation, but there is no gynaecomastia. Psychologically, he is a normal male and has been married for over a year. Intercourse has been achieved with some difficulty owing to the small size of the penis. Professor Barr has, however, reported that the nuclear picture in skin samples from both sides of the body is that of a normal female. The chromosomal determination is therefore at variance with the psychological sex.

Discussion

Diagnosis.—In many of the reported cases of true hermaphroditism the diagnosis was made incidentally during operation for other conditions such as hernia, or at post-mortem examination. The question of clinical diagnosis only arises in those patients brought for opinion because of genital malformation and consequent doubt about the sex. Such patients may be female or male pseudo-hermaphrodites or, much more rarely, true hermaphrodites. The female (adrenal) pseudo-hermaphrodite presents clinically with an enlarged clitoris and a uterus palpable on pelvic examination. There may be a history suggesting Addisonian crisis. The diagnosis is suggested by a raised urinary 17-ketosteroid level and confirmed by demonstration of enlarged adrenal glands, usually at laparotomy. The male pseudo-hermaphrodite or intersex with hypospadias and cryptorchidism will have no uterus and a normal urinary 17-ketosteroid level for his age. These two conditions may also be differentiated by examination of the epidermal nuclei, as outlined above. Most cases of true hermaphroditism have a uterus, and a phallus intermediate in size between penis and clitoris. The 17-ketosteroid level is, however, not raised. The diagnosis is made finally by laparotomy and biopsy of the gonads.

Classification.—From the published cases it appears that in true hermaphroditism either gonad may be a testis, an ovary, or ovotestis, independently of the condition found in the other gonad. The various possible combinations have been classified by Hinman (1935) as follows :

Type	One Side	Other Side	Reported Cases
Lateral	Testis	Ovary	22
Unilateral	Ovotestis	Ovary or testis	17
Bilateral	,,	Ovotestis	14
(Indeterminate)	,,	Not sectioned	8

It will be seen that Cases 1 and 2 reported here are lateral hermaphrodites and Case 3 is a bilateral hermaphrodite. In the majority of lateral cases reported the adnexae on each side corresponded to the gonad on that side. In the case of Brachetto-Brian *et al.* (1943) the asymmetry involved the whole body, one half being male and the other half female. In Cases 1 and 2 above, and that reported by Davis and Scheffey (1946), however, the abnormality was restricted to the gonads, the adnexae being female on both sides.

Aetiology.—The case mentioned above in which one-half of the body was male and the other female is analogous to the condition of gynandromorphism found in lower animals, such as insects and birds. Crew (1927) has shown that gynandromorphism in insects is due to loss of sex chromatin at the time of the first division of the fertilized ovum. It is well known that anomalies are not uncommon at this stage of development, such as the complete or partial separation of the primary cells which is thought to give rise to identical or conjoined twins. Since genetic maleness appears to depend on the absence of a second X chromosome rather than on the presence of the Y chromosome, the loss of one sex chromosome during the first division of the female zygote would result in one male and one female cell. It is possible that some such mechanism may operate in man. In the higher animals, however, sex may not be absolutely predetermined by the sex chromosomes, and the genetic direction of development may be overridden by other factors, of which hormones appear to be the most important. The relative significance of genetic, hormonal, and environmental factors in producing the many different varieties of human hermaphroditism is as yet unknown.

Management.—The major problem in the management of these cases is to decide on the predominant sex. In patients first diagnosed in adult life it is usually found that the emotions are appropriate to the sex of upbringing (the "social" sex) and that removal of the inappropriate gonad and suitable hormone therapy to reinforce the remaining gonadal tissue is satisfactory. In children, however, it is difficult to predict the direction the emotions will take at puberty. This is well shown in the case reported by Lattimer *et al.* (1943) and Engle *et al.* (1946). This patient had been brought up as a girl, but was masculine in behaviour. At the age of 11 an ovotestis and an ovary were removed, leaving a third gonad, which was thought to be a testis. The patient was then regarded as a boy, but at puberty three years later a strong female trend became apparent. The remaining gonad was removed (and proved to be an ovotestis) and the social sex changed back to female.

In Case 1 above, the parents were advised to bring up the child as a boy in view of the testis being much the larger gonad and the large size of the phallus, and in spite of the presence of female adnexae. This advice was reinforced by Professor Barr's opinion on the somatic nuclei. In consequence of this decision the hypospadias will be corrected at a later date.

The third patient mentioned above is psychically a normal male, although the epidermal nuclear picture is that of a female. It must be remembered that the patient has been treated with testosterone and also emotionally conditioned to some extent by his environment. Nevertheless it would appear that considerable caution is required when assessing the results of skin biopsy in true hermaphrodites. It is of interest in this connexion that 16 cases of true hermaphroditism have been social females and 41 social males (plus 2 neonatal cases), whereas skin biopsy on five true hermaphrodites has shown four with a female nuclear picture and only one with a male picture—Case 1 described above (M. L. Barr, 1954, personal communication).

Cases in the Literature

True hermaphroditism is probably less rare than the number of case reports might suggest. Several cases—for example, Photakis (1916) and Moriarty (1944)—were discovered by chance at post-mortem examination. Young (1937) collected 20 cases from the literature, to which McIver *et al.* (1944) added 11 others and two of their own. Greene *et al.* (1952) collected 48 cases and added one, and Fischer *et al.* (1952) collected 49 cases and added one. Two cases in the latter's list were, however, rejected by Greene (Stirling (1946)—"microscopy of testis unconvincing"; and Malgras and Gricouroff (1939) as ovarian tissue was deduced indirectly and not demonstrated histologically). Excluding these two cases, we are left with a net total of 53 cases. To these must be added six further cases : Broster *et al.* (1938), Berardinelli (1952), Brewer *et al.* (1952), Baker *et al.* (1953), Delore *et al.* (1953), and Laycock and Davies (1953). With the new cases reported here, the total number of acceptable cases is therefore 61.

Summary

Two cases of true lateral hermaphroditism are reported and the further progress of a third (bilateral) case is noted.

The first case presents the clinical problem of predicting the predominant psychological sex in adult life when true hermaphroditism is diagnosed in infancy. In this case the chromosomal sex, as determined by the method of Moore *et al.* (1953), was male, which agreed with the preponderance of male gonadal tissue. On the other hand, the third case cited has grown up a psychologically normal male, but the chromosomal sex is female. This suggests that the chromosomal determination of sex is of limited value in these cases and must

be considered in conjunction with all the available clinical evidence in deciding on the sex of upbringing.

The diagnosis of true hermaphroditism rests finally on the histology of the gonads, but a tentative diagnosis may be made on clinical grounds.

Fifty-nine previous cases of true hermaphroditism have been found in the literature. This small number is probably not a true indication of the real incidence of the condition.

I am indebted to Mr. L. R. Broster for permission to publish these cases under his care, and for his encouragement and help in the preparation of this paper. I have also to thank Dr. W. E. Evans and Professor M. L. Barr for reports on the sections.

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Medical Memoranda

Hair-grips as Foreign Bodies

The accidental swallowing of metallic foreign bodies by children is of everyday occurrence. The great majority pass through the gastro-intestinal tract without incident, being voided per anum in a few days, and, considering their size and shape, it is indeed remarkable how some manage to get through in tiny children without causing harm.

I would here like to draw attention to one variety of metallic foreign body commonly swallowed by young children—the familiar hair-grip. Hair-grips do not always pass through the gastro-intestinal tract with the same ease as the many other types of foreign body; sometimes they remain in the stomach or become impacted in the second part of the duodenum. This is particularly the case in very young children.

During the past ten years I have treated seven children with swallowed hair-grips and have had to resort to operation for the removal of the grip on four occasions. The four cases which came to operation comprised two girls and one boy, all under the age of 4 years, and one girl aged 7 years. The other three, all girls, were aged 4¼, 6½, and 13 years, and in these the grip was passed normally in a short space of time. Fig. 1 is a photograph of the four sizes of grip in common use, and it is the third largest size which is usually swallowed.

In children, particularly those under the age of 4 years, the grip tends to remain in the stomach, or, if it passes the pylorus, may become impacted vertically across the second part of the duodenum. Fig. 2 is an *x*-ray film showing the grip in such a position.

In two of the four cases which came to operation the grip was impacted across the duodenum, one child having swallowed the grip 17 days and the other 14 days before admission. The other two failed to pass the pylorus, one having been in the stomach five days and the other ten days before operation.

It is a simple matter to remove grips from the stomach, but nothing like so easy from the second part of the duodenum. In one of my two cases the grip was coaxed back into the stomach, and in the other it was coaxed onwards into the jejunum before removal, both being difficult manœuvres. However, I feel it is better to coax the grip

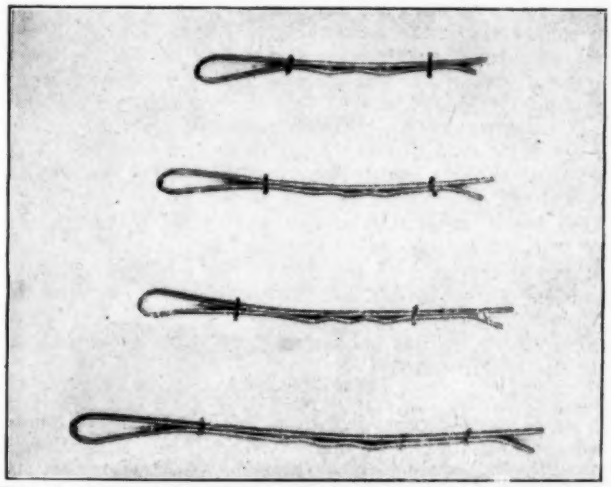

FIG. 1.—Photograph (actual size) of the four hair-grips in common use. The third largest is the one usually swallowed.

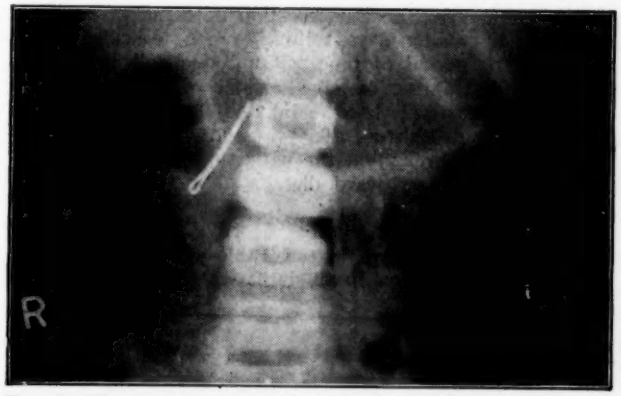

FIG. 2.—*X*-ray photograph of a grip impacted vertically in the second part of the duodenum in a girl aged 7 years. The gas-filled shadows of the stomach and colon can be clearly seen.

into an accessible region for removal than to open up or attempt to mobilize the second part of the duodenum in a young infant.

Prevention is better than cure, and mothers should be warned not to use grips for dressing young children's hair, but instead to employ the old-fashioned hair-slide with a large ornamental ring attached. It is the practice of the nursing staff of the children's surgical ward at the Royal Bucks Hospital, Aylesbury, to remove all hair-grips from young children on admission.

In those who have swallowed a hair-grip, treatment with a bulky diet and "normacol" is at once started, and *x*-ray films are taken of the whole abdomen at forty-eight-hour intervals to check progress. All stools are examined for the passage of the foreign body. In many cases emetics have been administered prior to admission to hospital in the

hope that the foreign body would be vomited, a dangerous practice when pointed or sharp objects have been swallowed. Furthermore, children who have swallowed foreign bodies should be admitted to hospital without delay so that skilled surgical treatment is at once available should the necessity arise.

The danger of delayed perforation by a hair-grip from pressure necrosis of the bowel wall will be only too apparent, especially if the grip has been impacted for any length of time.

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Effect of "Venostasin" on Serum Cholesterol Levels

In recent years attention has been drawn to the correlation in some instances between the serum cholesterol level and the occurrence of atheroma. The subject has been reviewed in the *Annals of Internal Medicine* (1950) and more recently by Gutman (1953). In 1953 Schimert and Schwarz reported that an extract of the horse chestnut, "venostasin," caused a significant reduction in the serum cholesterol level, which fell in 25 subjects from a mean level of 204 mg. per 100 ml. to 154 mg. after five daily intravenous injections of 5 ml. They found the extract inactive when given by mouth, but no toxic effects were noted after as many as 50 daily intravenous injections of 5 ml. each. The mode of action of venostasin is unknown, but if this effect is confirmed the material might prove of value in studying factors which influence the serum cholesterol level and in treating or preventing atheroma.

METHOD

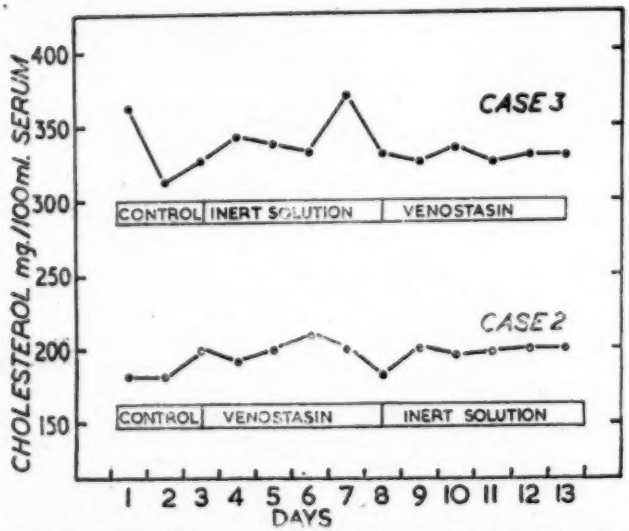
Six patients were studied by a "double-blind" technique using venostasin and an inert solution of burnt sugar indistinguishable in appearance from the venostasin. Neither the analyst nor the person giving the material knew whether the patient was receiving the horse chestnut extract or the inert solution. After a control period of three days the patients were given a daily injection of 5 ml. of one substance for five or ten days, followed by the other substance for a similar period of time. Blood was collected in the fasting state at approximately the same time each morning, and the cholesterol level estimated by a modification (MacIntyre and Ralston, 1954) of the method of Zlatkis *et al.* (1953). Throughout the period of study the patients received an ordinary ward diet.

RESULTS

The results are shown in the Table and two illustrative examples in the Figure. In all six patients venostasin had no detectable influence on the serum cholesterol level, whether this was in the high or in the low normal range.

Effect of Venostasin and an Inert Substance on the Serum Cholesterol Level

Case No.	Diagnosis	Average Cholesterol (mg./100 ml.)		
		Control Period	Venostasin Period	Inert Substance Period
1	Essential hypertension ..	193	191	193
2	Peptic ulcer	188	197	198
3	Coronary sclerosis ..	339	327	340
4	Essential hypertension ..	312	297	326
5	Coronary sclerosis ..	228	198	191
6	Mitral stenosis	183	201	218



Failure of venostasin or a solution of burnt sugar ("inert substance") to influence the serum cholesterol level in two patients.

We are indebted to Dr. R. I. S. Bayliss, at whose suggestion and on whose patients this investigation was carried out.

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Nitric Oxide Haemoglobin in Urine Due to Contamination

Nitric oxide haemoglobinaemia is probably incompatible with life. Banham, Haldane, and Savage (1925) described the finding of nitric oxide haemoglobin in the blood of a patient who died of pneumonia; they postulated a nitrifying organism in the blood as the agent producing the nitrification, though they did not confirm the identity of the abnormal pigment by spectroscopic examination. Barton (1954) described a fatal case of nitric oxide haemoglobinaemia due to sodium nitrite poisoning.

Nitric oxide haemoglobinuria has not been described. Below we report the identification of the pigment in urine, although the pigment was an artifact and not present in the patient.

A dark urine, which had been collected from a female patient in an open container eight hours previously, was examined in the laboratory. Nitric oxide haemoglobin was identified by spectroscopic and chemical tests (Harrison, 1947). As the patient was not desperately ill, but was suffering from stone in the urinary tract, the urine specimen was re-examined. It was found to be heavily infected with a mixed growth—one organism was a member of the Bacillus group. A catheter-specimen of urine was sterile. The mixed bacterial growth was cultivated in normal urine to which a little fresh blood had been added. The nitrifying action of the bacteria produced nitric oxide haemoglobin within 24 hours. The contaminated mixture was examined by a bacteriologist, but he was able to give a no more detailed identification than the one here presented.

The conclusion reached was that the patient's urine originally contained blood: the haemoglobin was converted to nitric oxide haemoglobin as a result of bacterial contamination from the faeces, the container, or the air.

We wish to thank Professor Sir Charles Dodds for his interest in this case.

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Reviews

OPERATIVE GYNAECOLOGY

Textbook of Operative Gynaecology. By Wilfred Shaw, M.A., M.D., F.R.C.S., F.R.C.O.G. (Pp. 444; 382 figures. £5.) London and Edinburgh: E. and S. Livingstone. 1954.

"Si monumentum requiris, circumspice"—these words, famed in other settings, could well be found on the title-page of this book. The author, whose contributions to gynaecological pathology and practice have made him famous, was in the front rank of modern teachers of obstetrics and gynaecology. His ambition to publish a *magnum opus* on gynaecology was half realized when he was stricken by a mortal illness. His active practice ceased, but, realizing that it was now a race with time, he laboured successfully with characteristic courage to complete the text of his book. Unfortunately, he did not live to see it published, or to correlate the manuscripts and illustrations—a task which was well completed by his junior colleague, Mr. John Howkins. This posthumous publication of a first edition is a great tribute to a distinguished and courageous man.

The early influence on the author of the Viennese school of Amreich and Werner is apparent throughout the book, and the debt owed to these masters is generously acknowledged. Mr. Shaw believed that in a textbook on operative technique the illustrations must be of the highest order. New blocks were made from some of the original pictures of Karl Hajek, and others were prepared from drawings by Erich Lepier; but most of the drawings with which the book is lavishly illustrated are the work of Mr. Leslie Caswell. These illustrations are of the highest standard and are an outstanding feature of the book. The captions are not always worthy of the drawings above them; for example, on page 181 the description of Fig. 126 refers to a left-sided hydrosalpinx when bilateral disease is portrayed, with no evidence of the adhesions referred to. On page 254, Fig. 190 illustrates a large enterocele which is described as a prolapse of the posterior vaginal wall. The drawings are, however, really superb, and their reproduction leaves nothing to be desired. They form a clear and permanent record of the technique Mr. Shaw adopted and taught.

A book so magnificently produced is necessarily expensive, and the prospective buyer must ask himself if it is worth the price. The answer will depend on what contribution he expects the book to make. If he wants a permanent visual record of how various gynaecological operations can be performed the money will be well spent; but surgery consists of much more than operative technique, and in the broadest sense this book is not a surgical guide. It reminds one of the student, harassed in a viva-voce examination, who when asked what treatment he would advise for menorrhagia due to fibroids seeks doubtful refuge in the evasive statement that "you can perform a subtotal hysterectomy, or perhaps a total hysterectomy, or possibly a myomectomy," and ends with the afterthought that "radiation might be used."

This book may not have a great appeal to those who have not had the good fortune to come under the personal influence of Mr. Shaw and who believe that surgery must be learned the hard way by apprenticeship to masters of experience and skill. For those who have been his students it should be in great demand as a beautiful record of the views and practice of an outstanding teacher.

JOHN STALLWORTHY.

PHYSIOLOGY AND BIOCHEMISTRY OF THE SKIN

Physiology and Biochemistry of the Skin. By Stephen Rothman, M.D. (Pp. 741+xiii; illustrated. £7 6s. 6d.) Chicago: The University Press. London: Cambridge University Press. 1954.

To review this book adequately would require the space allotted by the *Edinburgh Review* to Macaulay; for different reasons both editor and reviewer must plead *non possumus*. Suffice it to say that for dermatologists, and for many physiologists and biochemists, this book is of exceptional interest; nothing similar has previously been published in English. Unlike many promising ventures. there are no large gaps in the subject-matter and no amateurishness in the presentation. It is, in fact, the mature work of a senior man aided by seven collaborators, and most readers will appreciate that the subjects considered not only have been thought over in the study, the library, and the laboratory, but are presented with the assuredness and dexterity of the expert who has had frequently to lecture about and teach his subject.

A look at the table of contents is enough to reassure most prospective purchasers; a rapid glance through the pages reveals a sufficiency of diagrams, tables, and illustrations, and an adequacy of references.

Rothman has written 21 chapters; they vary in subject-matter from the mechanical properties and electrical behaviour of skin to epidermal proteins and lipid constituents. As was to be expected, he has contributed several chapters concerning sweat and a few on sebum. G. C. Wells writes about connective-tissue ground substance; Z. Felsher about collagen, reticulin, and elastin; A. L. Lorincz on pigmentation and nutrition; A. B. Lerner on enzymes; H. Pinkus on the biology of epidermal cells; and P. Flesch on the growth of hair.

If one requires facts they are here in plenty; their presentation is often brightened with interesting and valuable speculations and comments on the clinical application of the work under consideration. Further, the information is culled from international sources and is not merely an epitome of American work. In greeting this book one can be certain that it is but the first edition of a textbook which is certain to run to many editions.

R. M. B. MACKENNA.

COLLECTED PAPERS OF OTTO FENICHEL

The Collected Papers of Otto Fenichel. First Series. Collected and edited by Hanna Fenichel and David Rapaport. (Pp. 408+xiv. 35s.) London: Routledge and Kegan Paul Ltd. 1954.

Fenichel was from first to last the classical exponent of classical psycho-analysis in both its theoretical and its clinical aspects. His earlier published work, it is true, was perhaps governed a little too much by a respect for correct tradition, and, being also extremely compendious, suffered from lack of perspective and discrimination—a common failing among psycho-analysts. But these faults in presentation Fenichel gradually corrected; and he thoroughly deserved the international reputation he ultimately gained as a good clinician, a cautious theoretician, and a sound teacher.

This first volume of collected papers is arranged in chronological order and covers the years 1922–35 inclusive. It therefore gives the background of his earlier approach to psycho-analysis and its many theoretical and clinical problems. (Fenichel died in 1946.) Although the volume covers a wide range, the most important contributions to it are those dealing with the concepts of introjection and identification; infantile sexual theories and the aetiology of some perversions; the Oedipus complex and its pregenital antecedents, in particular the early sexual development of the girl; and the concept of defence against anxiety through libidinization. There is also an interesting paper on Freud's theory of the "death instinct," which Fenichel did not regard as of much heuristic value.

Fenichel was not a particularly original thinker or writer, and his boldest speculations concerned the concept of "respiratory introjection": though even here the credit for the concept of "respiratory erotism" belongs to the late David Forsyth. Nevertheless he is a persuasive writer, and this collection of papers should be obligatory reading for the psycho-analytical student. Although caviare to the general psychiatrist, it could also be perused with profit by his analytically minded confreres.

EDWARD GLOVER.

HORMONE RESEARCH

Recent Progress in Hormone Research: The Proceedings of the Laurentian Hormone Conference. Edited by Gregory Pincus. Volume X. (Pp. 511; illustrated. $9.80.) New York: Academic Press Inc. London: Academic Books Ltd. 1954.

This book records the proceedings of the tenth Laurentian Hormone Conference, which took place in September, 1953, in Quebec. The subjects discussed included hormone relationships and the nervous system, the physiology of thyroid hormones, comparative endocrinology, the chemistry of protein hormones, the relation of hormones to blood formation and destruction, and three aspects of clinical endocrinology. The discussions were, as usual, brisk, expert, and fully reported. Dr. Jack Gross and Mrs. Pitt-Rivers stated that thyroglobulin contains monoiodotyrosine and diiodotyrosine, thyroxine, and triiodothyronine. Thyroxine and triiodothyronine escape into the circulation, and then thyroxine is strongly bound to a specified protein, which is deiodinated at the target sites to enter the cells as triiodothyronine. Bernhard Zondek maintained that oestrogenic hormone is the regulator of the ovarian cycle, small continued doses initiating pituitary activity and large doses inhibiting it. By inserting a pellet of 20 mg. of oestradiol benzoate submucosally into the vagina, full function culminating in pregnancy was achieved in five patients with primary amenorrhoea and in thirteen with secondary amenorrhoea. Luft talked on electrolyte and fluid metabolism and discussed the results of hypophysectomy in the treatment of cancer of the breast and prostate and in diabetic retinopathy. It is too early to assess the therapeutic results of this operation; now, one year later, Luft finds the results of hypophysectomy in prostatic cancer more hopeful than in any other neoplasm.

The interesting physiological observation has emerged that it is possible to maintain for three or four weeks, without any substitution therapy whatever, patients who have undergone complete hypophysectomy: de Bodo compared this observation with the results in hypophysectomized dogs, which, despite consequent severe adrenocortical atrophy, were still able to conserve a sodium load normally.

Amidst much work that is of primary interest to biochemists this book contains a great deal which concerns the clinician.

D. V. HUBBLE.

CLINICAL NEUROLOGY

Textbook of the Nervous System—A Foundation for Clinical Neurology. By H. Chandler Elliott, M.A., Ph.D. Second edition. Introduction by Wilder Penfield, M.D. (Pp. 437+xx; 158 illustrations, and atlas of 50 plates. 72s.) London, Philadelphia, and Montreal: J. B. Lippincott Company. 1954.

This book has as its subtitle "A Foundation for Clinical Neurology," and it is essentially a textbook of the anatomy of the central and autonomic nervous systems as treated by the author, who is associate professor of anatomy at the University of Nebraska, in his lectures to medical students.

The arrangement of the book is unusual. The first section gives an outline account of the nervous system, and this is followed by a considerably longer section in which much fuller detail is included. This method naturally leads to a certain amount of repetition. The subject-matter is well handled and there is reference to function as well as to structure, which should make the book more interesting reading for a student. There are a large number of diagrams in the two sections, but some of them are rather difficult to understand. An unusual feature is an appendix of Latin and Greek words from which neuro-anatomical terms have been derived, and this should be useful, for, as the author says, "many students enter medicine without having been subjected to any Latin, much less Greek"—a state of affairs becoming more common in this country also.

The best feature of the book is the atlas of sections of the brain; this has been considerably enlarged since the first edition. Opposite each photograph is a line diagram on which are indicated the various structures potentially visible in the section, although it is by no means easy to recognize some of the structures so labelled.

J. W. ALDREN TURNER.

CARDIAC ENERGY

Myokardstoffwechsel und Herztherapie. By Dr. Med. Fritz Pendl. (Pp. 248+xii; 52 illustrations. D.M. 29.70.) Stuttgart: Georg Thieme. 1954.

The title of this book, which may be translated "Myocardial Metabolism and Cardiac Therapy," gives a very fair idea of its aims and scope. Though the subject is a difficult one, it is likely to become more and more important. After discussing the capacity of the human heart for work and describing the structure of the muscle cell, the author gives an interesting account of the origin of the cardiac energy. The part played by adenosine triphosphoric acid is fully dealt with.

In the next section is considered the influence of potassium, calcium, and sodium on the cardiac energy. Oedema and its treatment follow. Particular attention is given to the protection of the liver from damage so far as this is possible. There is a chapter on sugar metabolism, and the action of certain vitamins is considered.

Then finally the hormones are discussed. Each chapter has a full list of references and is provided with a practical summary. The matter is difficult and the expression is not always as clear as could be wished, but the author has made a very good attempt to present this most important subject in a way useful to the clinician. The emphasis on diet is greater than is usual in this country. Throughout the object has been to base therapy on a scientific foundation so far as present knowledge allows; the author points out how the study of these matters is still in a very early stage.

TERENCE EAST.

PERIMETRY

Perimetry. By Joshua Zuckerman, B.Sc., M.D., C.M., F.A.C.S. (Pp. 391+xxiv; 156 illustrations. 80s.) London, Philadelphia, Montreal: J. B. Lippincott Company. 1954.

A new volume on perimetry inevitably invites comparison with Traquair's book, and in the present instance a greater contrast in style could hardly be imagined. The economy and simplicity of Traquair are diametrically opposed to the reiteration and elaboration of this book.

Part I opens with a brief description of the usual appparatus employed in perimetry and continues with a dictionary of all the terms in common use, including brief notes on the pathological conditions which may produce field defects and the basic anatomy of the visual fibres. In Part II the instruments and technique are described in detail and the anatomy and physiology expanded. Normal and abnormal fields are then dealt with likewise. Part III is a summary at length of Part II and is followed by a tabular review of the whole book. Almost all the material is therefore presented some three times in varying arrangements and detail. For the duller student such a scheme may be useful, but it makes irritating reading for a practising ophthalmologist.

Disentangled from the reiteration, the substance of the book constitutes a good description of methods of examining the visual fields, of the anatomy and physiology of the visual paths, and of the field defects likely to be encountered in practice. There is little new matter, and a chapter on pitfalls in perimetry, containing some ninety items, fails to emphasize that the whole test is highly subjective and that elaborate perimetry is of no avail unless the patient is reasonably intelligent and co-operative.

E. S. PERKINS.

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PREVALENCE OF DYSENTERY

Since it became notifiable thirty-five years ago dysentery has shown great changes in both incidence and severity. Notification was introduced because soldiers returning to Britain brought with them this classical companion of the martial camp, but in time the number of cases reported declined, until in 1925 (345 cases) the nadir was reached. Thereafter a slow irregular rise brought the number of cases to roughly four times that figure by 1936. An explosive rise occurred in the autumn of 1937, when there was a threefold increase, and this level was continued in the following year but fell sharply in 1939. This proved to be the first of five great waves—1937 (4,167), 1941 (6,670), 1944 (13,025), 1950 (17,286), rising steeply to 28,590 in 1951. The uncorrected notifications for 1954 total 33,976. Three of these waves are separated by deep troughs, but the years of comparatively low incidence now show many more notifications than in any year preceding the first wave. Accompanying this vast increase in the number of cases reported each year is an equally remarkable diminution in virulence. In 1925, when notifications were fewest, the case fatality rate was nearly 40%: in the last two years for which complete figures are available it was 0.2%; and in the last five years, when the apparent spread has been so great, there has been an absolute fall in the number of deaths from dysentery. Although *Shigella sonnei* undoubtedly caused human infection earlier, it was first recognized in Britain in 1926; and this is perhaps of significance because in the recent epidemic years almost all of the confirmed cases have been due to this organism. In the years when prevalence is less the proportion of Sonne infections is lower. The changes in reported incidence and case mortality of dysentery can be explained by assuming that in the early years there was a fall in the incidence of the more severe Flexner dysentery and that the increase since 1925 represents the spread of the much milder Sonne infection, superimposed on a small, fairly static number of other infections.

Sonne dysentery is essentially a disease of temperate climates. Although *Shigella sonnei* has often been demonstrated in the Tropics, it is responsible there for only a small proportion of bacillary dysentery, and that this is not due to the milder infections being overlooked is shown by its relative infrequency in carrier surveys. That Sonne dysentery is also an infection which can spread rapidly where the standard of hygiene is relatively high we know to our cost in this country; and it differs from the majority of intestinal infections in being most common in the early months of the year. The frequency and extent of the spread of bacteriological infection in families, nurseries, and other institutions suggest that the infecting dose of *Shigella sonnei* is small. Compared with typhoid fever, in which the infecting dose is also small, the spread among contacts is much wider. Food-borne outbreaks of Sonne dysentery occur from time to time, but they are uncommon and do not account for more than a small proportion of the total cases. During an outbreak it is uncommon to discover a single common article of food, and *Shigella sonnei* has been isolated from foods much less frequently than the salmonella group of organisms, although the total Sonne infections greatly exceed the total salmonella infections. It seems preferable not to look on Sonne dysentery as a food-borne infection but to regard it as a "contagion," spreading directly from case to case with symptomless excretors and convalescent carriers playing some part. It is possible that the infection may also be passed on indirectly through infected fomites.

Most of the notified cases are in children, both of school age and under. Many outbreaks have been reported in schools, particularly in the infant classes, nursery schools, and day nurseries. Day nurseries in particular have been singled out as a possible source of infection of the general public, but there seems to be little to justify this view, since the decrease in the number of day nurseries since 1945 has not led to any fall in the reported incidence of the disease.

There seem to be real differences in the incidence of the disease both in time and in place. They are not fully accounted for by differences in diagnosis, notification policy, or laboratory facilities. In the large centres of population dysentery is probably always present. At some times it is confined to relatively small areas, not necessarily characterized by poor housing and overcrowding; at other times it spreads widely from these centres through the suburbs and into the surrounding countryside, but may miss completely many small and some large centres of population. The factors that determine whether the infection will spread widely or not are not well understood;

immunity of the population, housing conditions, social behaviour, even the weather may all play a part.

Almost all of the commoner bacteriological causes of human infectious disease have been split up in the laboratory into "types" by virtue of their different reactions to biochemical or serological tests or to different bacteriophages, and much of our precise knowledge of the way in which infections spread has been derived from a study of how the individual types spread. It has been possible to type strains of *Shigella sonnei* by a bacteriophage technique; but it has proved laborious to apply, the resulting types have not always proved stable epidemiologically, and the information gained has shown that the majority of all strains tested belong to a single type, so that we have not gained from this technique much additional insight into the way in which the organism spreads. Recent work on the distribution of sulphonamide-sensitive and resistant strains suggests that certain areas may well have their own individual infecting strains.

Sonne dysentery is not a very serious infection in man, yet it causes much discomfort and loss of working time and an appreciable number of severe and some fatal infections. The fatalities are mostly among the very young and the very old, debilitated by other conditions. It is a council of despair to recommend taking no action to prevent its spread, but we still lack sufficient knowledge to approach the problem in a practical way. To exclude all infected persons from school or work or from the society of their friends and neighbours entails more dislocation than the severity of the infection warrants. If we could recognize, as is possible to some extent in streptococcal infections, the dangerous carrier, a logical and practicable solution might perhaps be attainable, but at present all infected persons, young and old, with and without diarrhoea, have to be regarded as equally dangerous.

The widespread distribution in certain areas of strains resistant to sulphonamides suggests that chemoprophylaxis with these drugs can have but limited application, and the indiscriminate use of antibiotics cannot be recommended. Reports of outbreaks in schools provide some evidence that it is possible to control the spread of infection by excluding clinical cases and their home contacts from school, leaving the numerous symptomless excretors to continue to attend the school. Such action has the merit of being practicable. But much more experimental work is needed in schools, day nurseries, and other institutions before we learn how to control outbreaks effectively.

THE NATIONAL FORMULARY

A formulary provides a convenient collection of medical preparations for use in a community, and a national formulary reflects the prescribing habits of its country of origin. The existence of such formularies makes it unnecessary to prescribe a multiplicity of preparations with essentially the same composition and therapeutic value. The task of both prescriber and pharmacist is thereby eased and therapy is often made more efficient. The third edition of the *National Formulary—The National Formulary 1955*—is now being distributed and will be welcomed by all who have used its predecessors and have looked forward to an up-to-date version. Inevitably, however, its appearance in its present form will occasion criticism, for any volume so widely used by such a diversity of medical men is unlikely to meet with universal approbation.

Most ordinary prescribing demands can be met by the use of preparations included in the *Formulary*, which is admirably comprehensive and includes the more important effective modern therapeutic remedies. The new edition contains useful lists of those preparations which have been added to, and deleted from, the *National Formulary 1952*, and the substantial list of changes is a reflection of modern therapeutic advance with its recognition of the limited efficacy of many time-honoured remedies. It is therefore all the more surprising to find added to the formulary a number of preparations, especially mixtures, for which there is little therapeutic or pharmacological justification. They represent a concession to the extravagant lay and medical passion for a "bottle of medicine" and a reversion to the principles of Victorian and Edwardian polypharmacy. It is obligatory to prescribe only a strictly limited number of drugs—such as chloral hydrate or potassium citrate—in the form of mixtures, which are expensive compared with tablets and are a much less accurate way of prescribing medicines. It is therefore regrettable that an ammonia and senega mixture and a strychnine and iron mixture are added. The latter contains a negligible quantity of iron, but by its title may give the delusion of therapeutic efficacy. The inclusion of these formulae must represent the declared policy of the Joint Committee in the preface to include "a preparation, even if its justification on pharmacological grounds is disputed, if it is still being frequently prescribed." The committee has not always subscribed to this view, as, to quote the 1949 preface with regard to the exclusion of bismuth carbonate from antacid mixtures and powders, "The committee

realizes that these preparations are likely to be prescribed for some time to come, but it finds no evidence to show that bismuth carbonate has any advantage over, and should therefore replace, the analogous preparations which have been widely used in recent years and which are included in this formulary." This statement could be equally applied to several of the new formulae included in the 1955 edition. The new policy implies that the volume may be years behind contemporary advances in medical and therapeutic knowledge. The *National Formulary* is a potentially powerful and effective medium for the promulgation of good, sensible, and economic prescribing, and it should certainly have a more constructive function than that of slavishly following customs which may be ill-informed.

Major changes in the *British Pharmacopoeia 1953* were the substitution of English for Latin titles for monographs and drugs, and the use of the metric system for doses, imperial equivalents being quoted in brackets only where previously and traditionally used. The *National Formulary 1952* introduced English for the headings of subsections, despite the fact that in each section Latin titles were used for individual drugs. The arrangement of the sections was according to the alphabetical order of the English subsection headings, and this illogical compromise not unnaturally led to considerable confusion and irritation among users of the *Formulary*. The 1955 committee has taken what they realize will be regarded by a minority as a retrograde step, by deciding to revert to Latin for the titles of each group of preparations, and abbreviated Latin for the main title of individual preparations. This step will undoubtedly occasion some controversy. The committee has not seen fit to follow the lead of the *British Pharmacopoeia 1953*, and the *British Pharmaceutical Codex 1954*, and its refusal to follow such an authoritative lead may be a less reactionary step than some will undoubtedly think it is. The World Health Organization published in 1951 its *Pharmacopoea Internationalis*, and gave Latin names to the drugs listed in it, presumably on the highly sensible understanding that they would thus be readily recognized by users in the civilized world, and on the probable assumption that pharmacopoeias, at least in Europe, are in Latin. There is of course a practical side to this. Any national travelling or staying in a country not his own may need to have medicines prescribed by his home doctor dispensed by a foreign pharmacist: such a pharmacist should not have to cope with a vernacular prescription, or, for that matter, with a local system of weights and measures instead of the metric system. In the *Formulary* not only are metric equivalents quoted for the older galenicals which have been traditionally prescribed in imperial measures, but imperial doses are given, quite unnecessarily, for modern preparations such as isoniazid, digoxin, and methyl thiouracil which never have been and never will be either prescribed or dispensed in such a form.

The monographs at the beginning of the book are of a high standard and have been thoroughly revised. Those on antibiotics, sulphonamides, analgesics, and hypnotics are particularly good, but it is unfortunate that phenadoxone, an ineffective analgesic not included in the *Formulary* itself, will still retain the cachet derived from its mention in the monograph. A useful new section on anthelmintics has been added, and that on expectorants deleted, an omission which reflects the contemporary opinion that they are unnecessary and ineffectual, and which was forecast by the terms of the monograph in 1952. The index is of first importance, and great improvements have been incorporated. It is now most comprehensive, with many useful cross-references, and greatly increases the value of the volume.

The *National Formulary 1955* has manifest imperfections which can be regarded as inevitable in a work with such a heterogeneous parentage, there being no fewer than eleven bodies represented among the thirty-seven members of the Joint Committee. Nevertheless it will be found to be of great value and assistance in practice and in hospital. It is a pity, however, especially from the viewpoint of the education of the younger generation of doctors and medical students, that it contains features which will undoubtedly retard the development of sensible, honest, logical, and economical prescribing habits.

ERADICATION OF TUBERCULOSIS

Until recently the steady decline of tuberculous mortality remained unexplained except as a reflection of rising standards of living or as the declining phase of a long-term epidemic which was started by the industrial revolution. During the past ten years, however, miniature mass radiography (M.M.R.) has provided a means of finding unsuspected sources of infection and the antibacterial drugs have enormously strengthened the clinician's therapeutic powers—a subject on which we have recently commented.[1] The results upon tuberculosis mortality have been dramatic. During the last six years the annual decline in mortality from

respiratory tuberculosis has averaged 15%, while the average decline for the previous ten years was a mere 1.5%. But a falling mortality from a chronic disease may be accompanied by a rising prevalence, and of this we have no satisfactory index. The annual rate of notifiçation of new cases rose after the war, perhaps owing to mass miniature radiography, but in 1953 there was for the first time a decline in the figures despite increasing use of M.M.R. and increasing investigation of contacts,[2] so that it may be that morbidity as well as mortality is beginning to decline.

It is against this epidemiological background that the results (see p. 371) should be viewed of the first full deployment of medical resources against tuberculosis ever made in this country. The plan[3] was simple—to *x*-ray the lungs of the school and adult population of a coal-mining community in the Little Rhondda Valley (The Rhondda Fach). Every case of tuberculosis was thus to be discovered, all those with a positive sputum were to be treated—the Welsh Regional Hospital Board providing special wards for this purpose. If sputum conversion could not be achieved these patients were to be kept under rigorous supervision by a health visitor to deter them from spreading their infection. The effects upon morbidity and mortality from tuberculosis were to be assessed by periodic *x*-ray and Mantoux surveys. The paper by Drs. A. L. Cochrane, J. Glyn Cox, and T. Francis Jarman which we publish to-day gives some preliminary results from the first of these follow-up surveys. They show first that the plan succeeded technically, since 90% of the population were examined at each survey, and 95% of those *x*-rayed the first time were *x*-rayed again two and a half years later. This is an almost unique achievement.[4]

Four indices of the effects of the surveys are reported. First, there was a steep fall in the crude mortality rate from tuberculosis among the women and non-miners, a fall that was proportionately much greater than that experienced by the neighbouring part of the Rhondda or by the rest of England and Wales. There was at the same time a rise in tuberculosis mortality among miners, but this can reasonably be attributed to changes in the accuracy of death certification, and by the fact that tuberculosis in association with advanced pneumoconiosis is resistant to treatment. Secondly, the crude results of Mantoux-testings of schoolchildren suggest that the conversion rate must have been very low between the surveys, but a detailed report on this is to follow. Thirdly, the changes in the prevalence of tuberculosis are described. Large changes in such a chronic disease could not be expected, but, as a result of the treatment given, there was a notable decline in the prevalence of cases with a positive sputum, especially among the younger women; the decline was smaller among the men, and there was even an increase in the older men. After two and a half years 23.1% of the women and 41.7% of the men retained a positive sputum, the high rate of failure among the men being attributable largely to one quarter of the cases having advanced pneumoconiosis. These figures show that even to-day therapy cannot of itself be relied upon to control tuberculous infectivity.

The fourth and most important index was the attack rate of tuberculosis among those with normal radiographs in the first survey. At ages 15–24, it was 2.8% per annum for women and 4.7% for men, while at ages 25–34 it was 0.7% and 1.0% respectively. There was a negligible attack rate at later ages. This is the first time the attack rate of tuberculosis has ever been measured in a complete community in this country, so that it is impossible to say whether these are high or low figures; but a comparison with Springett's figures[5] for Civil Servants in London suggests that the Rhondda rates are low. A full analysis of the factors affecting the attack rate is to be published later. Meanwhile a hint has been given[6] that nearly all the new cases could be traced to contact with infectious cases before the latter were detected by the first survey and brought under control. If this is so, repeated surveys should undoubtedly achieve their object of reducing the attack rate to negligible levels and thus ultimately of abolishing tuberculosis from the community. One or two more surveys may be necessary, perhaps restricted to the younger age groups; and all known cases of tuberculosis (including massive fibrosis among the miners) will have to be followed to ensure that they do not become infectious.

The Rhondda Fach scheme is an example of epidemiology at its best, for the public benefits as research continues—research which is not confined only to tuberculosis and pneumoconiosis. Such diverse conditions as asthma, bronchitis, bronchiectasis, diabetes, hypertension, coronary artery disease, and rheumatism are also being investigated. Clinical research has been confined within the four walls of hospitals for too long. Pioneers such as the late Sir James Spence have led the way, and it is to be hoped that academic departments of medicine and surgery will increasingly undertake these field investigations as an essential activity. So far as tuberculosis is concerned the Rhondda survey has shown sufficient promise as a measure of preventive medicine to justify

[1] *British Medical Journal*, 1955, **1**, 273.
[2] Report of the Ministry of Health for the Year 1953, Part 2, page 96. H.M.S.O., London.
[3] *British Medical Journal*, 1952, **2**, 843.
[4] Cochrane, A. L., *Brit. med. Bull.*, 1954, **10**, 91.
[5] *British Medical Journal*, 1951, **2**, 144.
[6] *Quart. J. Med.*, 1954, **23**, 454.

any regional hospital board spending the necessary time and money to carry out pilot schemes of a similar nature. A clearer picture of the results which may be achieved will emerge when surveys have been carried out in areas where pneumoconiosis is not a complication.

FABRIC ARTERIAL IMPLANTS

Since 1912, when Carrel was awarded the Nobel Prize for his study of vascular transplants, there has been a steadily increasing literature on the subject which has appeared at a greatly increasing rate since the last war. Arterial replacement by means of autogenous vein grafts and arterial homografts was discussed in a recent leading article in this *Journal*.[1] The subject is again to the fore, for elsewhere in this issue Professor C. G. Rob and Mr. H. H. G. Eastcott describe the resection of an aortic aneurysm caused by tuberculous arteritis—a rare condition—with restoration of aortic continuity by an "orlon" prosthesis. It is certainly remarkable that a woven fabric identical with that used for clothing should be suitable for such a purpose. Blackemore and Voorhees[2] have already reported on the implantation of "vinyon N" cloth prostheses in eighteen patients, and Hufnagel[3] has also recently mentioned that he is using plastic cloths of various types to bridge arterial defects.

Many attempts have been made in the past to bridge arterial gaps with inert tubes, but they have all proved unsatisfactory, usually because of thrombosis or anastomotic leakage. With a porous fabric, however, fibroblasts from the surrounding tissues migrate between the interstices of the material to form a tough fibrous tube of living tissue. The fabric thus bears the entire burden of arterial pressure in the first few weeks only. At operation blood leaks through the pores in the cloth for a few seconds. The inner surface is covered with fibrin and polymorphs within a few hours, and acquires islands of endothelial cells which coalesce within three months. Blackemore and Voorhees, before using this method clinically, found that cloth implants in dogs remained satisfactory for periods of up to three years: thrombosis or leakage occurred in only seven of the thirty animals of the series. Encouraged by this success, they have used "vinyon N" tubes in seventeen patients with aortic aneurysms and in one with a popliteal aneurysm. There was a high operative mortality (40%) due to the technical difficulties of clamping and suturing the diseased aorta adjacent to the aneurysm. These hazards are present also when homografts are used. Ten of the seventeen patients survived the operation and all have remained well; the longest period of follow-up in any patient so far is ten months.

It is too soon to assess the final results of arterial reconstruction with grafts or fabric tubes. Homologous grafts often calcify and have been known to rupture. The only justification for introducing homologous tissue or foreign material into large blood vessels is when the life of the patient or a limb is in jeopardy. At the present time it is possible only to theorize on the relative merits of homografts and fabric tubes. Both are associated with the risk of rupture and thrombosis. As a rule the body ultimately rejects foreign material however inert it may be; the greatest use for it is as a scaffold on which living tissue can form, as in the repair of hernias with tantalum mesh. Such a process is claimed to take place around fabric tubes, so that it is immaterial if the fabric ultimately disintegrates by a process akin to metal fatigue. A word of caution is needed here, however, since collagen alone without elastic tissue can stretch. Collagenous tissue, artificially induced, not infrequently calcifies. Theoretically, then, fresh aneurysm formation and sudden rupture are still possibilities. The answer to this surgical problem should be available in ten years' time. In the meantime most surgeons will probably continue to use homografts, except when there is a special indication for a fabric implant. In the case reported by Rob and Eastcott there was a danger that an arterial homograft might become infected by the tuberculous tissue in the graft bed. In war surgery particularly fabric tubes would have the great advantage of availability and compactness: even if not a permanent solution to the problem of replacing wounded segments of major arteries they would be of great temporary value. If further laboratory and clinical experience eventually confirms that the results achieved by this method are permanently reliable, then, in the words of Brown and Hufnagel,[3] "most of the problems relating to procurement, processing, storage, and transportation of arterial grafts will be solved."

[1] *British Medical Journal*, 1954, **2**, 218.
[2] *Ann. Surg.*, 1954, **140**, 324.
[3] *J. Amer. med. Ass.*, 1955, **157**, 419.

IRON DEFICIENCY IN PREGNANCY

Blood is thicker than water, but less so in pregnancy. Varying figures are quoted, but W. L. Caton and his colleagues,[4] using radioactive isotopes, calculated that the total blood volume increased progressively in pregnancy by 45%, the peak being reached about the thirty-second week. The total number of red blood cells increased by about 40%, and the total amount of haemoglobin also rose. But a disproportionate increase of 55% in plasma volume caused haemodilution, so that the amount of haemoglobin per 100 ml. of plasma fell, producing the hydraemia or so-called physiological anaemia of pregnancy. A. S. Simpson[5] has recently pointed out that these factors make it difficult to interpret haemoglobin readings in pregnancy. He therefore also estimates the packed cell volume and thereby calculates the mean cell haemoglobin concentration. He contends that this concentration, which usually varies little through pregnancy, is the only reliable index of iron sufficiency, the critical level being 30.7%. Nevertheless, many clinical reports have been published over the last twenty years supporting the administration of iron to counter the usual fall

[4] Caton, W. L., *et al.*, *Amer. J. Obstet. Gynec.*, 1951, **61**, 1207.
[5] Simpson, A. S., *J. Obstet. Gynaec. Brit. Emp.*, 1954, **61**, 807.
[6] Benstead, N., and Theobald, G. W., *British Medical Journal*, 1952, **1**, 407.
[7] Davis, L. R., and Jennison, R. F., *J. Obstet. Gynaec. Brit. Emp.*, 1954, **61**, 103.
[8] Hamilton, H. G., *et al.*, *Sth. med. J. (Bghm, Ala.)*, 1953, **46**, 117.

in haemoglobin concentration in pregnancy. Among the more recent workers, for instance, N. Benstead and G. W. Theobald[6] and L. R. Davis and R. F. Jennison[7] have concluded that the so-called physiological anaemia of pregnancy is an indication of iron deficiency, and that an adequate intake of iron enables the concentration of haemoglobin normally found in non-pregnant women to be maintained throughout pregnancy. For maximum effect the oral iron must be taken from at least the twenty-fourth week.

On p. 385 of this issue of the *Journal* Drs. Mary Fisher and Rosemary Biggs offer further confirmation of this view. They carried out haemoglobin estimations on 104 pregnant women at the first antenatal attendance, at the twenty-eighth and thirty-eighth weeks, and also at the sixth week after delivery. They found that when the initial haemoglobin level was below 90% the administration of oral iron caused it to rise, while where the initial reading was over 90% this treatment maintained it at a high level. Twelve women did not respond to oral iron; in such cases the addition of ascorbic acid or dilute hydrochloric acid may be effective[8]; but it is doubtful whether the addition of molybdenum oxide is helpful. If there is no response to these preparations, and the patient is not suffering from the uncommon macrocytic anaemia of pregnancy, saccharated oxide of iron may be given intravenously or intramuscularly.

Drs. Fisher and Biggs remark that the clinical assessment of anaemia is highly fallacious, and they advise that, unless haemoglobin estimations can be done as a routine, oral iron should be prescribed for all pregnant women. They appreciate the difficulty of being sure that what is prescribed is really taken, but they claim that this treatment will probably avert dangerously low levels of haemoglobin. The attainment and maintenance of a high haemoglobin level during and after pregnancy not only increases the margin of safety for mother and foetus, but it also ensures the woman a quicker recovery from childbirth and gives her more energy to resume her household duties and to enjoy her motherhood.

ADMITTING TO HOSPITAL

Many general practitioners have had the frustrating experience of trying to persuade their local hospital to admit patients with certain disorders which do not, it seems, engage the hospital's interest. Typical of these are the victims of cerebral vascular accidents, about whom Dr. P. E. Brown writes at p. 382 of this week's *Journal*. He asserts that "those who do get admitted are often accepted with reluctance after tedious negotiations which are irritating to both house officers and practitioners." It is a familiar enough story, and some family doctors might admit that they have been driven to embellish the facts slightly in order to obtain an admission which they believed to be necessary: they may remember, too, the other side of the picture when they were residents in hospitals. Teaching hospitals naturally have to select patients in the interests of research and of teaching, and this gives the "interesting case" an advantage when it comes to admission, though cases can be interesting for other than purely academic reasons, and not least because they are the sort that make up much of general practice. But it is not only irremediable cases about which general hospitals are apt to raise difficulties. There are, too, the unfortunate bronchitics suffering winter exacerbations, the man with recurrent retention of urine, the obese old lady who unaccountably develops urinary incontinence, and the sick man from the common lodging-house, regarded with disfavour because he might be dirty and verminous. All may have a fair and urgent claim to a bed in hospital. Even old age itself is held to tell against a patient's need for admission. While discrimination is necessary in an imperfect world, the criteria that govern it deserve examination every so often lest the convenience of the hospital and its staff come to overbear the medical and social needs of the individual patients.

Some management committees, backed by medical opinion, may take the view that their first duty is to get the younger patient, the productive element in society, back to work, and that the elderly and the unemployable must take second place for hospital beds and other facilities. Economically, this is a reasonable view; by other standards it is surely hard-hearted. Anyhow, the need to care for an elderly relative in a sudden illness may keep an able-bodied man or woman away from work. Hospital staffs fear also that such patients will block the beds for a long time; if this happens, admitting house officers do not always find their seniors sympathetic. Dr. Brown's figures may not apply to all areas and in all circumstances, but they are enough to show that, for cases of cerebral vascular accident, this fear has no foundation. Energetic and early treatment of patients who have survived the first impact of a cerebral thrombosis, or of elderly people who have lately taken to their beds for one reason or another, often makes them fit to return to an independent existence. Yet if they are neglected for even a short while a serious long-stay problem may be created. But family doctors can help to ease the strain on hospital beds by careful selection of cases whose admission they seek. Brown's figures suggest the advisability, for instance, of not asking for admission of patients with cerebral vascular accidents until after the third day, if home conditions allow, when 30%—those with a hopeless prognosis—will have died whatever is done. Again, simple arteriosclerotic gangrene, a traditional reason for prompt admission, should perhaps not be regarded as so urgent a matter, for the disease in many cases progresses slowly.

Part of the solution to these problems is to set up properly constituted geriatric units with adequate medical and nursing staff, led by consultants, having their own admission wards, rehabilitation departments, and long-stay annexes, with access to the facilities of a general hospital. Such units, relieved of duties towards younger patients and patients with short illnesses, need not discriminate against the rest. General practitioners in the areas where they have been set up are relieved of many worries. The units sometimes have the additional satisfaction of counting among their successes just those cases which others have rejected.

EMERGENCIES IN GENERAL PRACTICE

SUDDEN OCCLUSION OF A MAJOR PERIPHERAL ARTERY

BY

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Sudden occlusion of an artery may be due to an injury, either open or closed, an arterial embolus, or an arterial thrombosis. Any artery in the body may be involved, but in this article only sudden occlusion of the major arteries supplying blood to the limbs is discussed.

This catastrophe does not necessarily imperil the life of the limb; in many patients the collateral circulation proves to be adequate. The popliteal artery has a particularly bad reputation and the incidence of amputation following sudden occlusion of the iliac, femoral, and axillary arteries is also high. But in the case of occlusion of other peripheral arteries gangrene is a rarity and the clinical effects often transitory, whilst slow occlusion of a vessel as large as the bifurcation of the abdominal aorta may produce surprisingly little disturbance. Eleven out of 26 of my patients with thrombosis of the aorta at this level are able to work on a medical regime of treatment, admittedly at only sedentary occupations.

Clinical Picture

A patient with sudden occlusion of a major peripheral artery calls in his doctor because the limb has become cold, pale, and perhaps numb, because agonizing pain has developed at rest, or because of the sudden onset of severe exercise pain (intermittent claudication). The severity of the symptoms varies with the rate of occlusion of the vessel, which means that they are usually more pronounced when the vessel has been blocked by an embolus than when it thromboses. There may be a previous history of intermittent claudication, a stroke, or angina pectoris, pointing to an arterial thrombosis as the reason for the new symptoms; or the patient may be suffering from auricular fibrillation or bacterial endocarditis, indicating that an embolus is the likely cause.

Pain is said to be a marked feature of an arterial embolus and usually absent when the blood flow has been interrupted by a thrombosis or an injury. This is on the whole true, but some patients develop no pain after an undoubted arterial embolus and others suffer agonizing pain from a thrombosis. Later the limb becomes numb, and, if gangrene is likely, the muscles can no longer contract and ischaemia of the nerve fibres leads to complete sensory and motor paralysis; in other patients gangrene is averted but severe rest pain develops.

The limb at first is pale and cold; in a severe case the skin looks and feels dead. Later the skin becomes cyanosed and, if gangrene is certain, a dark purple colour; usually areas of pallor are adjacent to areas of cyanosis, giving the skin a blotchy appearance. The temperature of the environment is of great importance both to the rate of onset of the various clinical signs and to the chances of recovery. If the part is kept cool, skin can withstand severe anoxia for 48 hours or more, muscle for 10 hours or so; nerve conduction ceases after about 30 minutes. Recovery from complete anoxia is much more likely after restoration of the blood flow if the part has been cooled. On the other hand, if the part has been warmed, blisters may form on the skin within 12 hours and muscle becomes gangrenous within a few hours.

The pulses are absent distal to the lesion and increased proximally. Thus a patient with a popliteal embolus will have no palpable pulsation in either the dorsalis pedis or posterior tibial arteries, but the popliteal artery will be unduly prominent because the embolus usually rests on the bifurcation of an artery and the main vessel above appears to pulsate more forcibly than on the normal side.

Treatment

There can be few emergencies which are influenced to a greater extent by good initial medical care than sudden occlusion of the main artery to a limb. Whilst admission to hospital should be obtained if possible, the first few hours are of great importance. Incurable changes can occur during this time. Simple measures taken in the patient's own home serve to minimize the effects of such a lesion. Unfortunately there can be no doubt that many patients with sudden arterial occlusion do not receive the best treatment. In particular, heating the limb by blankets or hot-water bottles does much harm. It can be stated that a patient who receives no treatment at all is better off than one whose limb has been either heated or elevated.

Treatment is discussed under the following headings: the reduction of the metabolic needs of the part; development of the collateral circulation; anticoagulants; maintenance of the patient's general health, and the prevention of infection and deformity; and surgical operations.

Reduction of the Metabolic Needs

This is best achieved by keeping the limb cool. It should not be frozen but exposed to the air at room temperature in temperate or cool climates or cooled by a fan in the Tropics. Cooling reduces cell metabolism and less oxygen is required, so that the part has a better chance of surviving until the blood flow is restored. Rest further reduces the metabolic needs; therefore active movements of the affected limb should be avoided and if necessary a light and well-padded splint applied. Rest may also be encouraged by the relief of pain, for which purpose pethidine, 100 to 150 mg., is usually more effective than morphine, ¼ gr. (16 mg.). For those patients with minimal pain a hypnotic such as amylobarbitone, 3 gr. (0.2 g.), is of value. A good drug for this purpose is alcohol; this often relieves the pain of sudden vascular occlusion, probably because it is an antispasmodic, and at the same time it helps the patient to sleep. One to 2 oz. (28–57 ml.) of whisky or brandy four-hourly is a satisfactory dose for these patients. It is important not to elevate the limb; the position of maximum comfort which most patients adopt in bed with the head and shoulders raised on two or three pillows and the trunk and limbs flat is also the best position for an ischaemic lower limb. Some patients obtain considerable relief when the limb is dependent; in acute vascular occlusion this may be allowed, but not for long periods.

Collateral Circulation

The development of the collateral circulation may be encouraged in a number of ways. The most efficient and at the same time the simplest measure is to establish reflex vasodilatation. To obtain this the affected part should be cooled and the rest of the body heated. With the patient in bed the method we use is to arrange the bedclothes in such a way that the affected limb is exposed to the air. The patient's other lower limb should be covered with a thick woollen sock, and both it and the trunk covered with blankets; a long-sleeved sweater and vest should be worn over the pyjama jacket and the hands in particular should be warmed; this is most easily achieved by asking the patient to wear a pair of woollen gloves, although electrically heated gloves are better if available. In the case

of sudden occlusion of a main artery to the upper limb, this limb should be cooled, and the feet, trunk, and other hand warmed.

Evidence produced by Sir Thomas Lewis and others has established that the vasodilatation produced in this way equals and possibly exceeds that of either a sympathectomy or a sympathetic nerve block. In some patients reflex vasodilatation worsens pain, but this often coincides with recovery of the circulation and is therefore a worth-while price to pay. This pain can be reduced by pethidine, 100 to 200 mg., or, if less severe, by tablets of codeine or aspirin.

It is important that splints, dressings, or the patient's posture should not constrict the region of vascular occlusion around which the collateral vessels must develop. Vasodilator drugs are of value, but in my opinion no proprietary preparation is superior to alcohol as a vasodilator in patients with sudden peripheral arterial occlusion; as already stated, this should be prescribed in liberal doses. Papaverine hydrochloride, ½ to 1 gr. (32–65 mg.), given intra-arterially, proximal to the lesion, may help to promote vasodilatation. Tobacco, on the other hand, causes peripheral vasoconstriction, and a wise patient stops smoking after sudden occlusion of a peripheral artery.

Sympathetic block with procaine hydrochloride or phenol is no better than reflex vasodilatation in promoting the development of the collateral circulation, but if performed with phenol it does enable some patients who would otherwise be bedridden to resume a sedentary occupation. It has no place in the treatment of an acutely ischaemic limb, but a real place in the treatment of elderly and poor-risk patients and of those who need prolonged sympathetic denervation but do not want a surgical operation. The technique consists in placing the patient on his side with the vertebral column straight, the third lumbar vertebra is located and a long (12-cm.) needle inserted at this level, and at a distance of 7 cm. (2¾ in.) from the midline; the needle should be directed inwards and advanced until it reaches the side of the body of the vertebra, it should then be manipulated until it slides forward to lie just in front of the convex antero-lateral surface of this bone. Aspiration serves to exclude the presence of blood or cerebrospinal fluid, and then 4 ml. of 4% procaine should be injected; if this produces a sympathetic block 10 ml. of 10% phenol in water is injected and the patient told to lie still for half an hour. This type of block produces a long-lasting sympathetic denervation.

Anticoagulants

Anticoagulants have an important place in the management of patients with sudden vascular occlusion. They help to limit the extension of the thrombus, particularly into the vessel distal to the block where the blood flow is sluggish. They should be used as a routine during the acute stage in all patients with sudden occlusion of the main artery to a limb, and for long periods afterwards in certain patients with arterial thromboses. Heparin, 15,000 units, should be given at once, preferably by intravenous injection, alternatively intramuscularly, and repeated six-hourly for 18 hours. At the same time phenylindanedione, 200 mg., by mouth, should be given and repeated twice daily in doses of 100 mg. Phenylindanedione takes about 18 hours to become effective, and so this combination of drugs produces a rapid effect which can be maintained for an indefinite period by the oral route. Control is by the prothrombin time; this should be reduced to give a prothrombin level of approximately 20% of normal in the acute phase and to about 30% or slightly more when long-term out-patient treatment is used. Most patients reach this level on a dose of 75 mg. twice daily, but some require only 50 mg., and others as much as 150 mg.

Phenylindanedione, once the dose has been stabilized, does not cause wide alterations in the prothrombin level and is therefore a relatively safe drug; once the level has become stabilized, weekly prothrombin estimations are sufficient for control. Should an overdose of heparin be given the antidote is an intravenous injection of 10 ml. of 1% protamine sulphate, and the antidote for phenylindanedione is 20 mg. of vitamin K_1 given orally. The above dosages for heparin and phenylindanedione refer to patients without a recent surgical or other wound. Both drugs are very difficult to control in patients with a recent wound, and should only be prescribed by those with considerable experience.

General Management

The general health of the patient must be maintained by ensuring an adequate intake of food and adequate sleep. Infection, an ever-present danger in ischaemic tissues, is best prevented by dressing all breaches in the skin with a careful aseptic technique and prescribing penicillin, 1,000,000 units twice daily, at the slightest sign that an infection is becoming established. Deformities may occur, particularly if a Volkmann type of contracture develops in the ischaemic muscle; these may be minimized by putting all joints through a full range of passive movement once a day. In some patients the ischaemic muscles are too painful to permit this. In these cases a light splint helps to prevent the development of gross deformities, particularly that of foot-drop.

Operative Treatment

Surgical operations, such as embolectomy, endarterectomy, arterial repair, or an arterial graft may succeed in restoring a normal blood flow. Others—for example, sympathectomy, incisions in the deep fascia, or arterectomy—may be used to assist the development of a collateral circulation. Alternatively, operation may be resorted to because conservative treatment has failed, when an amputation is necessary either for gangrene or for intolerable rest pain.

Embolectomy is rarely needed in the upper limb; the collateral circulation here is so efficient that the pulse usually returns to the wrist within 48 hours of a brachial embolus. On the other hand, embolic obstruction of the bifurcation of the abdominal aorta is best treated by immediate operation, as are many embolic obstructions of the popliteal or common femoral arteries. A great deal depends upon the appearance of the limb; in many patients the blood flow is returning by the time the patient reaches hospital, and conservative treatment with anticoagulants and reflex vasodilatation alone is effective; however, where there are good facilities popliteal or common femoral embolectomy usually pays, for by this means a normal blood flow can be restored. Arterial repair and arterial grafting have their most important indication in those patients with sudden arterial occlusion due to an injury; of obvious importance in war, these injuries when they occur in peacetime require adequate surgical treatment. For example, I have seen in the last two years three butchers who had accidentally divided their femoral arteries with their own knives; in one an end-to-end suture was possible, and in the other two an arterial graft was necessary; all now have patent vessels with a good blood flow and palpable pulses distal to the lesion.

Sympathectomy is of great value after the acute phase has passed; before this it has a place in those patients who cannot tolerate reflex vasodilatation. The object of the operation is to increase the collateral circulation around the occluded artery; therefore, those ganglia which control the appropriate area of the patient's vascular tree should be removed. For example, removal of the second and third lumbar ganglia denervates the patient from the knee downwards, and when the first lumbar ganglion has been removed the denervated area includes the upper thigh. In addition, sympathectomy makes the skin warm and dry—a valuable contribution to the welfare of a patient with an ischaemic limb. The other two operations designed to assist the development of the collateral circulation—arterectomy and incisions in the deep fascia—have in my view little real value.

Amputation, whilst being a last resort, should not be unduly delayed in patients with rest pain. The level varies

with the level of occlusion in the arterial tree and the efficiency of the collateral circulation. With experience, many patients can receive the added benefit of a conservative operation, but in others a major above-knee amputation is required. The important thing is to obtain primary healing of the skin flaps and a stump which is useful.

Conclusion

Sudden occlusion of a major peripheral artery is an emergency the outcome of which depends to a large extent upon the initial care which the patient receives. The importance of local cooling, reflex vasodilatation, and anticoagulants has been stressed. The ideal to aim at is restoration of the blood flow to normal, but this is not often possible. The alternative is to encourage the development of an efficient collateral circulation.

Next article on Emergencies in General Practice.—"Crises in Myxoedema," by Dr. Richard Asher.

Refresher Course Books.—Copies of the first two volumes of collected articles from the Refresher Course for General Practitioners published in the *Journal* are still available at 25s. (postage 1s.) each. The first volume contains 55 articles and the second 60. Each article has been revised and brought up to date by its author.

These books may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

LEGAL LIABILITY OF DOCTORS

In the fourth of his series of lectures* at the City of London College on February 2, Mr. J. P. EDDY, Q.C., discussed the liability of doctors, hospitals, and dentists to actions for negligence. In recent years, he said, there had been a considerable increase in the number of actions brought against doctors and hospitals. Figures provided by the Ministry of Health showed that payments by hospital authorities in England and Wales by way of compensation of all kinds amounted in 1948–9 to £7,500, in 1950 to £23,000, in 1951 to £38,000, in 1952 to £106,000, and in 1953 to £153,000. The causes of this increase of litigation were: (1) the changed status of the hospital; (2) the payment of hospital staffs; (3) the availability of free legal aid; and (4) the decision of the Court of Appeal under which hospital authorities were responsible for the negligence of their staffs.

Changed Status of the Hospital

Formerly many members of the community devoted much time, thought, and energy to the welfare of the hospital, which was regarded as "our" hospital. Nowadays they were not taking the same personal interest and the hospitals were regarded as State hospitals. Consultants and other members of the hospital staff were formerly not paid or were paid such a modest sum that it might be described as an honorarium. Nowadays consultants, registrars, and house officers were paid a salary; they were appointees, or indeed employees of hospital management committees or regional hospital boards or boards of governors.

Again, the legal-aid scheme had made it possible for members of the public to institute actions against doctors or hospital authorities or both. The committees charged with the duty of issuing legal-aid certificates had been doing their work well, taking reasonable care to satisfy themselves that a prima-facie case existed before issuing a certificate. Where there was an allegation of negligence against a doctor or hospital a medical report was called for. In Scotland the prospective litigant had an opportunity of being heard before a certificate was granted. Mr. Eddy did not think that that was desirable; there should be nothing in the nature of a preliminary trial, it was enough that there was a prima-facie case.

Finally, the decision of the Court of Appeal in *Cassidy* v. *Ministry of Health* (1951, 2 K.B 343) had transformed the legal position in regard to liability of hospitals for negligence on the part of their medical staffs.

Duty of the Doctor

The duty owed by a doctor to his patient was laid down in 1838 in the case of *Lanphier* v. *Phipos*. A doctor undertook to bring to the exercise of his profession a reasonable degree of care and skill, but before the duty arose there must exist the relationship of doctor and patient. If a doctor saw a person lying injured in the street and passed him by he was not guilty of negligence, because there was no such relationship and consequently he owed no duty; but if he played the part of a good Samaritan the professional relationship was created, even though the doctor had no hope of reward. Moreover, he was liable only when he undertook the treatment of a person, not when he merely examined him at the request of someone else. A doctor incurred liability when he set out to treat a patient, but not when he expressed an opinion at the request of another person (1920, 3 K.B. 163).

In the *British Encyclopaedia of Medical Practice*, Dr. Walter Levitt, pointing out that the doctor must exercise a reasonable degree of care and skill, added:

> "What is a competent degree of skill will depend on the circumstances in which the practitioner finds himself. If he practises in a remote village, away from modern sources of inspiration and knowledge, very much less will be expected of him than if he practises in a large town attached to a hospital with every possible convenience and inducement for keeping his knowledge up to date."

The duty of warning the patient of possible danger in the treatment to be undertaken was pointed out in the judgment in *Clarke* v. *Adams* (1950, 94 *Sol. Jo.*, 599). In an earlier action in 1934, in which the patient complained that a hypodermic needle had broken and been left in her tissues, the defendant claimed that the breaking was due to muscular spasm on the part of the patient, and the judge, while finding that there was no negligence, came to the conclusion that the doctor should have told the patient of the accident. The patient was awarded five guineas damages. Mr. Eddy cited other cases which turned upon the adequacy of the warning given to the patient.

Hospital Liability

In 1906, in the case of *Evans* v. *Liverpool Corporation* (1 K.B. 160) the plaintiff claimed damages on the ground that his son had been discharged from an infectious diseases hospital while still in an infectious condition and had communicated scarlet fever to his other children. It was held that the plaintiff was not entitled to recover, for the legal obligation of the defendants extended only to the provision of reasonably skilled and competent medical attendance. To-day beyond any question the hospital would have been held liable.

Mr. Eddy mentioned the cases of *Lindsey C.C.* v. *Marshall* (1937, A.C. 97) and of *Gold* v. *Essex C.C.* (1942, 2 K.B. 293). The latter did much to clarify the legal position. It turned upon the failure of a radiographer adequately to protect a child's face when Grenz rays were being given. Mr. Justice Tucker held that the defendants were not liable for negligence, but an appeal succeeded, and it was held that a whole-time servant of the hospital, in failing to provide adequate screening material, rendered the hospital liable.

But it was the decision of the Court of Appeal in the Cassidy case, already cited, which was one of the reasons for the increased litigation to-day. This was a case originally tried by Mr. Justice Streatfeild at Liverpool Assizes. The patient, suffering from a contracture, had been treated in a Liverpool hospital, and in the treatment his arm had

*The first lecture was reported in the *Journal* of January 22, p. 221.

been kept rigid in a splint for several days. When it was released it was found that the hand was to all intents and purposes useless. The case went to the Court of Appeal, and there Lord Justice Singleton said that it was clear that there was negligence in the post-operative treatment. He also pointed out that it was not possible for the patient to say that the negligence was that of any particular individual; it might be that a number of people were at fault or that lack of system was the cause. The responsibility lay upon the hospital. Lord Justice Denning said:

"If a man goes to a doctor because he is ill no one doubts that the doctor must exercise reasonable care and skill in his treatment of him, and that is so whether the doctor is paid for his services or not. But if the doctor is unable to treat the man himself and sends him to hospital, are not the hospital authorities then under a duty of care for their treatment of him? I think they are. . . . Why should it make any difference if he does not pay them (the hospital) directly, but only indirectly through the rates which he pays to the local authority or through insurance contributions which he makes in order to get the treatment?"

Lord Justice Denning also pointed out that, since the hospitals had no ears to listen through the stethoscope and no hands to hold the surgeon's knife, they must do it by the staff which they employed, and if the staff was negligent in giving the treatment the hospitals were as liable for that negligence as was anyone else who employed others to do his duties for him. This seemed all so clear that one wondered why there should have been any doubt about it, yet for over thirty years it was the general opinion of the profession that hospital authorities were not liable for the negligence of their staff in the course of their professional duties. When a doctor or surgeon, whether consultant or not, was employed and paid not by the patient but by the hospital authorities, he was of opinion that the hospital authorities were liable for his negligence in treating the patient. It did not depend on whether the contract under which he was employed was a contract of service or a contract for services.

Mr. Eddy went on to mention the case of *Jones* v. *Manchester Corporation* (1952 2 Q.B. 852) in which Mr. Justice Oliver found the doctor guilty of negligence in the administration of thiopentone to a patient who had been already anaesthetized. In this case the responsibility was apportioned as to 20% on the doctor and 80% on the hospital board. In the Court of Appeal Lord Justice Denning said in this case that the hospital board had no right to indemnity or contribution from any member of its staff except in so far as the court thought it just and equitable having regard to the extent of the person's responsibility for the damage.

After reviewing some other recent cases Mr. Eddy concluded this part of his lecture by again quoting Lord Justice Denning to the effect that the term "consultant" did not denote a particular relation between a doctor and hospital; it was merely a title denoting a place in the hierarchy of the hospital staff. The consultant was a senior member of the staff, but just as much a member of the staff as a house-surgeon.

Reports of Societies

STRIPPING OPERATION FOR VARICOSE VEINS

On February 2 the Surgical Section of the Royal Society of Medicine met to hear three papers, one of them by Professor J. B. KINMONTH on his experience of the stripping operation for varicose veins.

Professor Kinmonth explained that the operation of stripping varicose veins was not new. In the second century Galen avulsed them with a hook. At the beginning of this century the procedure was rediscovered by Keller, Mayo, Babcock, and others. After the first world war the injection of sclerosing solutions came into vogue and stripping went out of fashion, and it was not until 1947 that the operation again became popular with the work of Myers. The design of the stripper had varied. Keller in 1905 used a length of wire which turned the vein inside out, and Mayo in the following year invented an extraluminal instrument similar to a tendon stripper. Babcock in 1907 used a rigid wire with an olive head, and Myers modified this by making the wire flexible. This was the instrument in use to-day.

Professor Kinmonth said that he preferred to strip the saphenous vein from below upwards, having first carried out a standard Trendelenburg operation at the groin. He made a transverse incision at the ankle and at the knee, and the vein was removed in two lengths, using a small stripper below the knee, since it was less traumatic and less likely to damage the saphenous nerve. When necessary both legs were treated at one operation. The commonest complication was haematoma formation, and various precautions were taken to prevent this: the operation was carried out in the Trendelenburg position, and a sterile Esmarch's bandage was applied as the vein was stripped and let *in situ* until the wounds were sutured. After the operation, wool and crêpe were applied and the Trendelenburg position was maintained for some hours.

Complications

The feared complications of stripping varicose veins were thrombosis and pulmonary embolism. Accordingly Professor Kinmonth made his patients walk the day after operation, and crêpe bandages remained in place for a month. In fact the danger of pulmonary embolism was no greater than in general surgical operations as a whole, and occurred in about 0.5% of cases. In a series of 204 stripping operations at St. Thomas's Hospital there had been one case. At St. Bartholomew's Hospital there was one case in 157 operations, and at University College Hospital one case in 237 operations. None of these were fatal. Similar figures have been reported from the Mayo Clinic. In 1950 Murley had reported that in a series of general surgical operations performed at St. Bartholomew's Hospital, where special precautions were taken, there were 6 cases of pulmonary embolism in 1,289 patients, an incidence of 0.5%, and at the Mayo Clinic the figures were similar. Professor Kinmonth felt that the results of the stripping operation for varicose veins was very satisfactory, and, although statistical evidence was almost impossible to obtain because of the nature of the condition, recurrences were fewer than with other forms of treatment.

In the ensuing discussion Mr. F. B. COCKETT stated that at the vein clinic at St. Thomas's Hospital stripping had become a routine operation in the moderate and severe cases, since it gave better results than other methods and reduced the operating time. He pointed out that ablating the saphenous vein did not necessarily interfere with all the perforating veins, especially near the ankle.

Mr. J. B. OLDHAM stressed the importance of conservative treatment for varicose veins and the division of all tributaries at the sapheno-femoral junction when doing the Trendelenburg operation. He felt that, although there was no one single operation which cured varicose veins, the stripping operation was the most promising so far. Concerning the technique, he advised a vertical incision at the ankle and application of strips of adhesive felt along the course of the vein as it was removed. Mr. H. DODD stated that he operated on one leg at a time because of the danger of venous thrombosis. He noted that the operation was singularly free from discomfort. The results were good, and in consequence post-operative injections of sclerosants were rarely necessary.

Professor KINMONTH, in replying to a question from Professor C. G. ROB, said that he occasionally stripped the short saphenous vein, but that it was not often worth while. He concluded by saying that the operation of stripping varicose veins did not cure the condition, and he told the patients so.

LOCAL MEDICAL SOCIETIES

MANCHESTER MEDICAL SOCIETY

At a joint meeting of the Sections of Medicine and Pathology on January 12 Professor C. H. GRAY gave an account of "Some Clinical Studies of Urinary Adrenal Steroids."

He said that although there was evidence that the physiologically important hormones secreted by the adrenal gland were hydrocortisone, corticosterone, aldosterone, and two androgens, a very much larger number of substances chemically related to these were excreted in the urine. Some might perhaps be intermediates in the synthesis of the important steroids in the adrenal gland which had leaked out in small quantities. Others, however, were metabolites of the active hormones. It was small wonder, therefore, that the earlier methods of determining adrenocortical steroid hormones in urine had been unsatisfactory, either because of lack of specificity or because they estimate some functional group common to a number of metabolites. Separation and estimation of all the adrenal metabolites in urine was necessary for a complete picture but would tax the time and energy of a mammoth institute.

Hormone Assays in Endocrine Disorders

The estimation of cortisone, hydrocortisone, and tetrahydrocortisone by paper chromatography seemed to be of value in the diagnosis of hypoadrenalism, continued Professor Gray, although these three metabolites accounted for only an extremely small fraction of endogenous or exogenously administered adrenal hormones. In both Addison's and Simmonds's diseases the excretion of these three compounds was greatly reduced, and might not be measurable in many patients with the former disease. In Simmonds's disease administration of A.C.T.H. restored the excretion to normal limits. The appearance of hydrocortisone in the urine after administration of cortisone, and of cortisone after administration of hydrocortisone, to patients with Addison's disease or after adrenalectomy showed that hydrocortisone and cortisone were freely interconvertible in the body even in the absence of the adrenals. The proportions of cortisone, hydrocortisone, and tetrahydrocortisone in the urine were approximately the same whichever hormone was administered. There was no doubt that cortisone and hydrocortisone were therapeutically equivalent, except possibly when some local action was required, as with some ophthalmological and joint conditions.

Some, but not all, cases of Cushing's disease showed an increased excretion of hydrocortisone, cortisone, and tetrahydrocortisone. When the total excretion of these three compounds was within normal limits, the excretion of either cortisone or hydrocortisone might be increased, suggesting that delayed inactivation of the active hormones might sometimes be an important factor in Cushing's disease. In other cases, however, none of these metabolites was increased, and, while it was possible that in these the adrenocortical hormones might be metabolized to a greater extent via other pathways, it was not impossible that in this disease phases of normal activity and of overactivity of the adrenal gland might alternate. Perhaps hypersensitivity of the tissues also played some part.

The excretion of cortisone, hydrocortisone, and tetrahydrocortisone was not increased during salicylate therapy, so that unless there was an alteration of the metabolism of the adrenocortical hormone from normal it seemed unlikely that salicylates produced their therapeutic effect by stimulating the pituitary adrenal axis.

North of England Obstetrical and Gynaecological Society

At the annual general meeting in Manchester on January 21 the following officers were elected for 1955: *President*, Mr. H. J. MALKIN (Nottingham); *hon. treasurer*, Mr. C. H. WALSH (Liverpool); *hon. general secretary*, Mr. J. B. COCHRANE (Nottingham); *hon. reporting secretary*, Miss U. M. LISTER (Leeds).

Nova et Vetera

THE ILLNESS OF EDWARD THE BLACK PRINCE

Edward the Black Prince seems to have enjoyed good health up to 1366 (including his successful campaigns in France), and led an active, vigorous, and warlike life. His ill-health dates from his unfortunate expedition to Spain, undertaken to restore Don Pedro the Cruel to the throne of Castile. In 1366, when the Prince was at Valladolid waiting in vain for the promised money from King Pedro, "his army suffered so terribly from dysentery and other diseases that it is said that scarcely one Englishman out of five ever saw England again."[1] "The army also were half-starved, and the free companions in the prince's pay ravaged the country."

The Prince contracted a severe and debilitating illness, which lasted for ten years. It was probably amoebic dysentery which merged into the chronic form, for there are contemporary references to his dysentery subsequently. Sir George McRobert informs me that amoebic dysentery still occurs in Spain as well as the bacillary forms. In 1369, when the Prince was at war with Charles V of France, Froissart states that his health was so feeble that he could not take an active part: he was swollen with dropsy and could not ride. Oedema of the legs and ascites have been noted in dysentery due to anaemia caused by intestinal haemorrhage. Alternatively, the Prince's dropsy may have been due to chronic nephritis, which sometimes complicates dysentery. A third suggestion is that it was a "hunger oedema," due to semi-starvation in Spain. The first explanation seems the most probable one.

In 1370 Charles V of France raised armies for the invasion of Aquitaine. Though ill, the Prince left his sick bed in Angoulême, gathered an army at Cognac, and sacked Limoges. A sick man, he was carried in a litter.

In January, 1371, on the advice of his physicians, he returned to England and went to his manor of Berkhampstead "ruined in health and fortune." His health improved, presumably with rest and dieting. In August, 1372, he sailed on an expedition with King Edward III, his father, to relieve Thouars, but the fleet, exposed to contrary winds for nine weeks, eventually returned without landing on the French coast.

Later, "the Prince's sickness became very heavy." He knew he was dying, was much in prayer, and did many good and charitable works. "His dysentery became very violent, and he often fainted from weakness, so that his household believed he was actually dead."[2 3 4]

This was the result of the severe dysenteric haemorrhages and associated weakness and anaemia.

The Prince eventually died from dysentery and exhaustion in 1376, aged 46. His body was brought from the Palace of Westminster to Canterbury and buried with great state in the Cathedral.

ARTHUR S. MACNALTY.

[1] Knighton, H. In *Historiae Anglicanae Scriptores Decem*, edited by R. Trysden, col. 2629. London, 1652.
[2] *Chronicon Angliae*, pref. XXIX, p. 88. London, 1874.
[3] Chandos, the Herald. *Le Prince Noir*, edited by F. Michel, line 4133. London, 1883.
[4] Hunt, W. *Dictionary of National Biography*, vol. 17. 1889.

In her Annual Report for the year 1953 Dr. Catherine B. Crane, medical officer of health of the city of York, reports that attendances at the antenatal clinics, apart from midwives' clinics, were negligible, because the major part of the antenatal work in York is carried out by the patient's own doctor in domiciliary cases and by the hospital staff in cases booked for hospital confinement. "This we welcome," Dr. Crane writes, "provided adequate antenatal teaching can be given."

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Agranulocytosis

SIR,—In an annotation[1] you recommended that A.C.T.H. or cortisone should form a routine addition to the standard treatment of drug-induced agranulocytosis, though with a warning that not all cases might respond. This view was based on the reports of two cases of agranulocytosis in Canada[2] and U.S.A.[3] respectively which, caused by sulphonamides, were successfully treated with A.C.T.H., and a case reported in the *Journal*[4] caused by "novalgin" and treated with A.C.T.H. with recovery. Further cases of drug-induced agranulocytosis have been since reported in your *Journal*[5,6] and elsewhere,[7–9] in which A.C.T.H. was considered to have aided recovery. The use of A.C.T.H. in the treatment of agranulocytosis caused by drugs has also been referred to in a standard textbook.[10]

The potential danger of amidopyrine as a cause of agranulocytosis is well known, and certain related proprietary preparations—for example, novalgin—carry the same risk; for this reason the latter has been placed on Schedule 4. The case reported in the *Journal* (January 22, p. 207) by Drs. H. E. Hutchison and Hugh Conway died of an embolus five days after admission after improvement had occurred on antibiotics alone. As corticotropin and cortisone were not mentioned in their note we felt that attention should be directed to a form of therapy which is occasionally of great assistance in drug-induced agranulocytosis.—We are, etc.,

D. G. WRAITH.
F. DUDLEY HART.

London, W.1.

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2 Caldwell, A. L., *et al.* (1950). *Canad. med. Ass. J.*, **62**, 506.
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10 Wolvius, R. J. (1953). *Ned. T. Geneesk.*, **97**, 2183.

Disk Lesions and Low Backache

SIR,—The paper by Dr. James Cyriax (*Journal*, January 15, p. 140) and the letter from Mr. John Charnley (p. 163) illustrate the difference of opinion—not to say confusion of thought—about these conditions, granted that there is a larger field for the use of manipulation. Dr. Cyriax is altogether too facile in regarding the great majority of patients suffering from lumbago and sciatica as subjects in some degree of disk lesion. The diagnosis of disk lesion is not as easy as all that. What does it rest on? (*a*) A history of injury or sudden onset (but many a case gives neither); (*b*) pain which on strict analysis is truly acute, with confirming clinical signs of local spasm and sciatica; (*c*) some element of confirmation by *x*-ray. With many others, I have had the misfortune to perform laminectomy at several levels in the "certain" case, only to find no evidence of disk protrusion. *X*-ray films often show no evidence of diminution of the intervertebral space, and, conversely, gross diminution may appear in films taken for some other condition—for example, the flat film of a barium series—with no complaint from the patient of lumbago or sciatica. It should be remembered that the intervertebral articulation comprises three elements—the disk, the spinal ligaments, and the apophyseal joints—and that any pathological condition which affects one affects all.

The late Dr. H. A. Cookson examined 22 patients at necropsy, none of whom in life gave any history of backache or sciatica; of these, eight showed obvious disk protrusions, apparently symptomless. In operating for disk lesions, the apophyseal joints when examined consistently show pathological evidence of osteo-arthritis, degeneration of hyaline cartilage, capsular thickening, and resultant narrowing of the channels through which the nerve roots emerge, especially that of the 4th lumbar. My personal view is that this condition is more frequently the source of lumbago-sciatica than minor disk protrusions.

Dr. Cyriax stresses fairly the value of manipulation and traction; Mr. Charnley recognizes the value of psychological concord with the patient, but rightly dreads the prospect of a multiplication of the physiotherapy services. May I suggest a method of treatment which effects the first and obviates the second? It is not original; it was put forward in a clinical lecture on scoliosis by that shrewd observer the late Professor Alexis Thompson, in 1909. The patient hangs from a ladder, arms fully extended, head retracted, knees bent up: in this position he hyperextends the pelvis on the lumbar spine, then swings from side to side. In the home a ladder is not normally available, but the top of a door is, and makes a good substitute. Having reached the limit of tolerance, he now lowers himself carefully to the four-foot position, and crawls round the room half a dozen times. If sciatica is present, he crawls away from the affected limb, as in Klapp's exercise, the hand and knee being approximated on the contralateral side. A firm pillow, 12 in. (30 cm.) square, is strapped to the lumbar area, and the patient instructed to repeat the routine, at least once daily. Thick gloves should be worn, and the knees protected by cotton-wool pads.

This procedure is effective in the great majority of patients, and not infrequently dramatic; it has the advantage of simplicity, it can be repeated *ad lib.* by the patient, and throws little strain on the physiotherapist or the overwrought orthopaedic surgeon. Most important, it emphasizes the principle that what the patient does for himself is worth a ton of what someone else, lay or medical, does for him. I use injections very little—when I do, I give 5 ml. of lactic acid, *without procaine*, paravertebrally on either side, trying to reach the root of the lumbar transverse process at the appropriate joint. Most procaine preparations, being hydrochlorides, have a *p*H on the acid side. —I am, etc.,

Sunderland. W. GRANT WAUGH.

SIR,—For many years now I have been carrying out Dr. James Cyriax's methods of diagnosing and treating low backache. This I have done in general practice. I would therefore like to give my figures for a twelve months' period, in reply to the request of Mr. W. D. Coltart and Mr. H. Osmond-Clarke in their letter (*Journal*, January 29, p. 288). I would like to add that these patients could not easily hide their recurrent backaches from me, as I was their N.H.S. doctor and they could not therefore seek advice elsewhere, as suggested by Dr. D. M. Freeman (p. 289), and very few complain that the treatment was painful.

	No.	%
Cases treated	185	
Considered suitable for manipulative reduction	133	
Relieved in one session		57
,, ,, two sessions		19½
,, ,, three ,,		1
,, ,, four ,,		6
,, ,, traction		9
Referred to St. Thomas's Hospital		7
Recurrences		20
Cases considered suitable for traction	52	
Relieved in 1–5 treatments		43
,, ,, 6–10 ,,		23
,, ,, more than 10, or referred		35

I consider that these results substantiate the claims made by Dr. Cyriax. I should add that many of the treatments were given by my physiotherapist. I think it is a pity that so many of our noble profession criticize his methods, without having a working knowledge of them. Those who do watch the diagnosis being worked out, and the treatment being carried out, are usually enthusiastic.—I am, etc.,

London, W.1. R. BARBOR.

SIR,—Mr. John Charnley (*Journal*, January 15, p. 163) defends the orthopaedic surgeon's approach towards the problem of chronic low backache. Unfortunately only a small percentage of genuine derangements of the musculo-ligamentary-skeletal structure of the lower back can be demonstrated by *x*-ray or any other scientific investigation. Nevertheless, they are the undoubted cause of a great deal of chronic invalidism and most of them can be cured by simple manipulation. The Cyriax traction is an aid—but I prefer to use my hands. I must confess that I sympathize with the patient who, having been sent from one specialist to another and from one *x*-ray department to another, says that nothing has been done for him, for nothing has in fact been done to relieve him of his backache, which is after all what he has asked for.

Simple manipulation does not require an anaesthetic, takes only a few minutes of the manipulator's time, and the question of expense does not arise, since the only equipment necessary is a couch and a pair of trained and confident hands. I still hope that we are approaching the day when the profession will at last realize the value of this type of manipulation and will accept it whole-heartedly.—I am, etc.,

London, S.W.16. HARRIS AVERY.

SIR,—In his article on spinal disk lesions (*Journal*, January 15, p. 140) Dr. James Cyriax states that manipulation of the spine should not be in the hands of "lay manipulators." Yet that is the very thing he does by relegating this work to physiotherapists. The American osteopaths have a far superior training to the physiotherapists, and, in fact, the training of those recognized by the British Osteopathic Association compares very favourably with that given by many of the medical schools in every way. These osteopaths are recognized by the United States Government, and in many cases have to pass the same State Board Examination as the medical graduates before they can practise.

Manipulation of the spine is an extremely skilled work. It is true that anyone can be taught the necessary movements, but the application of the manipulation is the important thing, and this cannot be taught nor can it be relegated to those who have not had the thorough training that an American osteopath has had. There must be definite reasoning, ingenuity, the requisite skill, and, above all, the ability to apply the manipulation. It cannot be left to those who have not had considerable experience. There are some osteopaths who are just "joint crackers," and they are the ones who throw discredit on the true osteopaths. There are many physiotherapists who are just "skin rubbers," but that does not mean that there are not many who fill a very necessary need. American osteopaths, however, are taught manipulation from every angle, and in so many cases each manipulation must be reasoned out. There can never be any stereotyped method of manipulating a spine. The variations of restricted movement of the spinal joints are so numerous that unless the treatment is correctly applied there can be no certainty of the outcome and, what is more, the patient may be worse. This work cannot be accomplished unless one knows how and why.

What is a disk lesion in its early stage? Is not this the osteopathic lesion? Apart from this definite and simple cause, there is no other reason for what are styled disk lesions. Are they disk lesions? Has the medical profession ever improved upon the manipulations of the osteopath? It has copied them and imitated them, and claimed them as original, but there the comparison ends.—I am, etc.,

Newcastle-upon-Tyne, 2. R. W. R. WATSON.

SIR,—I have read the correspondence on the treatment of low back pain with very great interest. From my own experience I can state that a modification of Dr. James Cyriax's method does work. The patient who is brought to an out-patient department by ambulance, in such severe pain that he cannot stand or walk, can be relieved so rapidly that he can walk to hospital next day, and return to work within a week.

This very fact raises doubts in my mind as to the diagnosis. From the consideration of the anatomy of a lumbar intervertebral disk, it is hard to believe that a herniation of the nucleus pulposus or a tear of the ligamentum annulare can be "replaced" so that they remain in position. Is it not more likely that these acute cases are really lesions of the interlaminar joints, possibly a subluxation? Weight is given to this view by the fact that the majority of these acute cases are caused by a flexion and a rotation strain. Might it not be well to reserve the diagnosis of a disk lesion for those cases with sciatic pain and/or neurological signs?—I am, etc.,

London, W.1. A. C. ELKIN.

Tonsillectomy

SIR,—Following the article by Dr. Christine M. Rendell on the premedication of children for tonsillectomy (*Journal*, December 11, 1954, p. 1397) there has been varied and interesting correspondence. I do not propose to comment on this, but rather on a fact which has been mentioned *en passant*, and which may be of interest to posterity: the fact that guillotine tonsillectomies were still being performed in large numbers in the second half of the twentieth century—*circa* 1955.

In May, 1909, there appeared in the *Lancet* an article of extreme clarity and simplicity by George Waugh,[1] then senior surgeon to out-patients at the Hospital for Sick Children, Great Ormond Street. This paper, which dealt with "A simple operation for the complete removal of tonsils, with notes on 900 cases," was destined to revolutionize the surgical treatment of chronic tonsillitis. Of the 900 cases mentioned 143 had already had their tonsils guillotined, some of them as often as two or three times. I quote verbatim: "It is probably a common experience of all large out-patient departments—and certainly of my own at Great Ormond Street—to find a large number of patients upon whom tonsillotomy has been performed and to whom no relief either of the local or general condition for which the operation was done has resulted. From the frequency with which the operation has been repeated, sometimes as often as three times, and from the fact that the operation has been performed by many operators at other hospitals in these 143 cases, it seems right to conclude that the cause of failure lies not with the operator but with the type of operation. Even in highly skilled and experienced hands the complete removal of a tonsil by means of the guillotine is a task of such mechanical difficulty as to be, except in a few rare cases, quite impossible."

Waugh was accustomed to seeing many patients who had been subject to inadequate, inaccurate surgery. To-day, 46 years later, the same type of patient continues to attend the clinics, with huge masses of infected tonsillar remnant, and in some cases a deficiency of uvula, faucial pillars, or soft palate suggesting that these innocent anatomical structures must have been indicted and sentenced to mutilation along with the tonsils and adenoids. Guillotine apologists advance the following arguments: long waiting-lists preclude the performance of the dissection operation in every case, but this more lengthy, deliberate, and precise operation may be reserved for cases in which pre-operative findings are suggestive of adherent tonsils. In some centres the post-operative haemorrhage rate is higher in dissected than in guillotined cases: a longer anaesthetic is necessary for the dissection operation: but perhaps the most dangerous and frequently repeated platitude of all is that in the hands of experts the guillotine operation gives satisfactory results. I hasten to agree, but expert guillotinists are few.

Not one of these reasons is valid. A lengthy waiting-list cannot be said to justify any technique other than the best. Which method would the surgeon wish in the case of his own child? Of course the post-operative haemorrhage rate is higher following the removal of abnormally adherent tonsils, and if dissection is reserved for these cases any comparison of the haemorrhage rates following the two methods is bound to give rise to fallacious conclusions. As regards the length of anaesthetic, I think most of us would agree that anaesthetists have not been the least progressive of our colleagues, and the era when operation-time was reduced to a minimum in order to curtail their activities has long since passed.

I anticipate much opposition to the view that the guillotine operation should be relegated to the historical section of every textbook, but let me make it quite clear that I am in no way critical of those revered colleagues who for many years have employed the method with diligence and success. But rather, in the words of Waugh, "The cause of failure lies not with the operator but with the type of operation."—I am, etc.,

London, W.1. E. H. MILES FOXEN.

REFERENCE

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Carcinogens in Cigarette Smoke

SIR,—The interesting point made by Professor R. D. Passey (*Journal*, December 18, 1954, p. 1485) referring to the prolonged exposure of the skin of the fingers of cigarette smokers to the products of the combustion of tobacco has often puzzled me. It has occurred to me that one possible explanation might be related to the relative absence of sebaceous follicles in the skin of the finger-tips (of course, this does not apply in the case of the lip or the eyebrows). The skin of young mice devoid of sebaceous follicles was shown to be resistant to the carcinogenic action of methylcholanthrene by Lacassagne and Latarjet,[1] and I have failed over a period of many years to induce any epithelial tumours in the skin of fowls with a variety of chemical carcinogens that are potent for the skin of mice. One of the peculiarities of the skin of the domestic fowl is an absence of sebaceous follicles except in the preening glands. Another and simpler explanation would be that the products of combustion of cigarette smoke are not carcinogenic for human skin.

I make these comments without prejudice in regard to the possible carcinogenic action of cigarette smoke on the epithelium of the bronchus and lung.—I am, etc.,

Glasgow, C.3. P. R. PEACOCK.

REFERENCE

[1] *Cancer Res.*, 1946, **6**, 183.

Obstruction from Orange Pith

SIR,—One of the disadvantages of being in a distant part of the Commonwealth is that the *Journal* takes so long to reach us. I have only recently received the numbers in which your correspondents discuss the dangers of orange pith (*Journal*, November 27, 1954, p. 1301, and December 18, p. 1484). I, too, have had an experience with the fruit which I think merits recording.

On March 20, 1951, I was urgently requested to see a coloured male child aged 4 years at the Coronation Hospital, Johannesburg. This child had been treated recumbent in a Jones's frame for four months for a tuberculous lesion of the 8th thoracic vertebra. He had been perfectly well until 7.30 p.m. that day, when a nurse had noticed the child was struggling for breath. The houseman was called and diagnosed acute tracheal obstruction, and, as I happened to be in the building, asked me to see the child. When seen at 7.45 p.m., the patient was semiconscious and deeply cyanosed. Rib recession was marked and the accessory respiratory muscles were contracting forcefully. Air entry into both lungs was scarcely audible. It was presumed that a foreign body had been inhaled and an immediate bronchoscopy was performed in the ward without anaesthesia. No difficulty was experienced in introducing the instrument, but intense bronchial spasm was produced which lasted only a short while and was followed by total flaccidity, unconsciousness, and an impalpable pulse. A rapid cursory inspection of the main bronchi failed to reveal the presence of a foreign body. The bronchoscope was withdrawn into the trachea and the lungs inflated with oxygen. While we were debating whether the heart had stopped the houseman jubilantly reported the return of feeble radial pulsations. Within a few minutes the child was pink and the heart beats forceful. Trichlorethylene was then administered to the now struggling child and a more leisurely inspection of the bronchi failed to produce the expected foreign body. The bronchoscope was then slowly withdrawn, and it was noticed that the upper tracheal lumen was reduced to a slit by an extratracheal mass projecting from behind. As soon as the instrument was withdrawn into the larynx the obstruction recurred. Nothing had been noticed during the hasty introduction of the instrument; no bar to its advancement had been met. The bronchoscope was again pushed beyond the obstruction and with a laryngoscope the interarytenoid fold was lifted forwards. A mass of white cotton-like material was seen to be impacted in the lower pharynx and on withdrawal was found to be a mass of orange pith. A considerable quantity was removed, which must have extended for some distance down the oesophagus. This completely relieved the tracheal obstruction. I subsequently learned that the child had eaten an orange about an hour before the tracheal obstruction was first noticed.

One wonders whether the bolus lodged in the pharynx and oesophagus had slowly increased in size by absorption of saliva and other fluids until eventually the soft trachea was sufficiently compressed to impede breathing, or whether actual difficulty had been experienced for an hour before it was eventually noted. I was assured that the child had shown no signs of restlessness after his evening meal and had certainly made no complaint.—I am, etc.,

Johannesburg. PAUL MARCHAND.

Silver Stool Sign

SIR,—Sir Heneage Ogilvie's description (*Journal*, January 22, p. 208) of this condition in cancer of the ampulla of Vater is very important. It may be of interest to report that we have occasionally received silver stools from young children convalescing from diarrhoea. We have assumed, but without proof, that sulphonamide or other medicaments were responsible for this odd appearance.—I am, etc.,

London, N.9. M. E. M. THOMAS.

SIR,—It was with considerable interest that I read Sir Heneage Ogilvie's medical memorandum on "Thomas's Sign, or the Silver Stool in Cancer of the Ampulla of Vater" (*Journal*, January 22, p. 208).

A 65-year-old patient was admitted to hospital in the early hours of December 25, 1954, with abdominal pain and vomiting of over 24 hours' duration. He was found to have a paralytic ileus and peripheral circulatory failure due to peritonitis. Although there was much discussion about the cause of the peritonitis, the most likely one was considered to be a perforated peptic ulcer. He was treated conservatively and never really became fit enough for laparotomy. During the course of his illness he passed quite a definite "silver stool." My wife, who happened to be the ward sister at the time, stated that she had been taught that "silver stools" were characteristic of pancreatic disease. I consulted several surgical and medical colleagues, as well as the professor of pathology, and none had met the use of the term "silver stools" in pancreatic disease, or in any other condition. On being referred to a textbook of nursing[1] I found the statement that "in some diseases of the pancreas the stools have a silvery appearance." The patient referred to above died on December 30, 1954, and necropsy revealed gross haemorrhagic pancreatitis.

In view of this case I respectfully suggest that this is not the first description of "silver stools." Also, "silver stools" are not really diagnostic of carcinoma of the ampulla of Vater and can evidently occur in other diseases of the pancreas.—I am, etc.,

Manchester, 13. W. J. METCALFE.

REFERENCE

[1] Riddell, M. S. (1938). *Lectures to Nurses*, 7th ed. Faber and Faber, London.

SIR,—Sir Heneage Ogilvie's memorandum entitled "Thomas's Sign, or the Silver Stool in Cancer of the Ampulla of Vater" (*Journal*, January 22, p. 208) immediately attracted my attention, as I have once observed the phenomenon which he describes, but was not aware of the significance which he attributes to it.

The patient was a diabetic man aged 68 years who had been jaundiced for five weeks as a result of obstruction of his common bile duct by a large stone. He was passing clay-coloured motions at the time when he was first seen. At operation the stone was removed from the grossly dilated common duct, which was then drained with a rubber catheter. The patient's condition was very poor and he developed a profuse biliary fistula around the tube

and died of bronchopneumonia a few days after the operation. On the morning of his death the sister of the ward called my attention to a stool which the patient had just passed and which had been saved because neither she nor the staff-nurse had ever seen anything resembling it. It was a bulky well-formed stool which resembled exactly, in colour and appearance, the aluminium paint which is commonly sprayed on pipes and radiators. It was not merely grey in colour but had a definite metallic lustre. I was at a loss to explain the phenomenon but had a colour photograph of the specimen taken, and, as it was not repeated, was unable to investigate it further.

If, as Sir Heneage says, the phenomenon is due to the presence of altered blood in the pale stool of obstructive jaundice, then the origin of the bleeding in my case was no doubt the operative trauma to the common bile duct. Sir Heneage suggests the passing of silver stools may be an important sign in the diagnosis of carcinoma of the ampulla of Vater: one wonders whether it will be of much practical value. In the first place I suspect that the phenomenon must be very rare, as I cannot imagine the passage of stools, the colour of the one that I have described, escaping notice and comment by the nurses and the ward sisters. In the second place, surely the existence of unexplained obstructive jaundice is in itself an adequate reason for surgical exploration, and, as Sir Heneage has mentioned, the source of the haemorrhage which may be responsible for the silver stools is not necessarily from the obstructive lesion itself. It would be interesting to know whether others have observed the phenomenon of silver stools, and if they have I hope that they will write making their observations available.—I am, etc.,

Cardiff. ARNOLD S. ALDIS.

Alcohol as a Diuretic

SIR,—I was shocked to detect my revered ex-teacher of clinical medicine in an error both of fact and implication. In Professor L. J. Witts's review of the third series of "Any Questions?" (*Journal*, January 29, p. 271) he invokes Shakespeare to his support in his contention that alcohol is a diuretic. He quotes a reference which I cannot verify, as my copy of *Macbeth* shows Act II to have but two scenes. If he refers to the conversation between Macduff and the porter in Scene I, then what does Shakespeare say?

Porter.—Faith, Sir, we were carousing till the second cock: and drink, Sir, is a great provoker of three things.
Macduff.—What three things does drink especially provoke?
Porter.—Marry, Sir, nose-painting, sleep, and urine.

Will he quote an authority who supports the outworn theory that excessive drinking causes a red nose? What, I wonder, did the porter at Inverness castle drink? Unless he can be shown to have ingested pure alcohol, then Professor Witts's contention is vain, for most drinks contain other ingredients—for example, ol. juniperi—which may well be specific diuretics.

All the good Will Shakespeare says is that if you drink much you pass much urine, and that can hardly be denied.—I am, etc.,

Wellesbourne, Warwick. LAWRENCE MACKIE.

Hypodermic Injection Technique

SIR,—When, as a student at St. Thomas's, I had my first lesson in the use of the hypodermic syringe it was impressed on me that never under any circumstances should the plunger be depressed without a previous withdrawal to ensure that the needle had not entered the lumen of a dilated venule. I have withdrawn the plunger in every injection I have ever given since then, and in the course of thirty years I have withdrawn blood on at least five or six occasions. Depending on the drug or serum used, each of these half-dozen cases might have been a fatality.

I am astonished to find that no nurses I come across have been taught this elementary safety-first precaution. Surely so simple a thing should be drilled into everybody who handles this ubiquitous, but nevertheless potentially lethal, weapon.—I am, etc.,

St. Ives, Cornwall. L. P. LOCKHART.

Dyspareunia

SIR,—Mr. G. W. Theobald (*Journal*, January 22, p. 228) suggests that Mr. R. Christie-Brown (*Journal*, January 8, p. 106) might find his new dyspareunia clinic unnecessary (for the relief of infertility) if he would try cauterizing the internal os uteri with a stick of silver nitrate, which he believes "would cure most cases of dyspareunia provoked by deep penetration of the penis." But if the infertile patient's cervical anatomy and physiology happen to be normal, what then? Might not the stick of nitrate change all this?

I would rather see the dyspareunia clinic abandoned for other reasons. I agree whole-heartedly with Mr. Oswald Lloyd (*Journal*, January 22, p. 228) that "these cases are a challenge to the patience and ingenuity of the non-surgical aspect of our specialty" and, like him, I regard as unfortunate the present tendency to hive off into component clinics various groups of gynaecological disorders. The groups selected are usually those less spectacular conditions which require time-consuming histories, investigations and/or treatments; they are, in fact, the very cases which need mature clinical judgment in their handling to bring maximum benefit to the patient. Unfortunately, such cases interfere with the *tempo* of the conveyer-belt system of out-patient departments, so dear to the heart of the lay administrator these days.

The herding together of similar cases into clinics may be an administrative expediency and may be justified for the purposes of research and the collecting of data, but it is good neither for the patients themselves nor those who staff them (and how often is this work delegated to juniors?). Both are apt to develop distorted ideas. In short, unless the patient derives maximum benefit from her visit to the hospital, what appears to be administrative efficiency is, in fact, the reverse.—I am, etc.,

South Shields. TERENCE ROBINSON.

What is Health?

SIR,—I read with great interest Dr. A. H. Macklin's letter (*Journal*, January 22, p. 229) in which he set out certain constructive criticisms of the Kent Paediatric Society's report[1] and gave a few details of the 10-year survey at present being carried out in the University of Aberdeen.

In undertaking a mathematical assessment of health, the Society was well aware of the difficulties and dangers of such an approach and appreciates that the method set out in the study represents but a first step in the evolution of a generally acceptable standard. Indeed, it is hoped that not only the marking form but all the other measurements will be studied and improved upon by other workers in this field. As one reviewer has put it,[2] "The modern locomotive engineer may laugh at some of the original crudities of the first productions of Watts and Boulton, but without their work there could have been no Flying Scotsman." Although we are, yet, by no means convinced that health *can* be measured, we hope that this analogy may prove to be a sound one.

It may be that surveys based on the correlation of factors applied to individuals in special groups by methods of observation and record may yield satisfactory results; but the fact that such surveys take ten or more years reduces considerably their usefulness in field trials, where a more rapid assessment is desirable. Besides, the subjective element in such surveys is very strong and it is not always those whose "all-round qualities" appear to be outstanding who deserve to be placed in the highest category of health; the dark horse has always to be reckoned with. Neither do such methods lend themselves to standardization, which alone would permit of their universal application.

The assessment of personality or character is, perhaps, the most important (and certainly the most fallible) aspect of health assessment, for on character may depend the power of the individual to rise above physical or even intellectual disability. Health, in the absolute sense of "wholeness," can rarely, if ever, be a human attribute, and the most that we can aim at is the highest degree of well-being which can result from the individual's

endowment of physique, intelligence, and character. Any method of assessment must take into account this compensatory mechanism. How would a Franklin D. Roosevelt or a Helen Keller be placed in the Aberdeen survey, or the Kent survey for that matter? Certainly the latter could and should be modified to ensure that these would not be rejected from the category of health.

Even the "intelligent, highly reactive personality" must, somehow, come to terms with his environment by a process of mutual interaction, failing which the result can only be withdrawal, which may well be an element in psychopathology. This may be the reason why genius is so often associated with disease and must therefore be regarded as abnormal. It is, of course, not necessarily the "healthy" who contribute most to human advancement, and, indeed, the reverse may be the case; but health must not, on this account, be thought of as a state of dull, uninspired mediocrity. The stability of society may well depend on "normal," "healthy" people, and it is the aim of the infant science of "hygiology" to be able to recognize health, if possible to measure it and to discover its causes. For has not health its specific causes no less than disease? The results of the Aberdeen survey may shed much light on some of these problems.—I am, etc.,

JOHN LANDON,
Chairman, Kent Paediatric Society Research Subcommittee.

Bexleyheath.

REFERENCES

[1] *A Study in the Epidemiology of Health*, published from the Health Department, 14, Brampton Road, Bexleyheath, Kent.
[2] *Med. Press*, 1954, **232**, 533.

Cortisone, A.C.T.H., and Asthma

SIR,—Your annotation on this subject (*Journal*, January 22, p. 216) deserves comment. During the last few years I have treated 28 asthmatic patients with A.C.T.H. or cortisone with a high percentage of pronounced improvements. This result does not differ from those of Dr. J. E. G. Pearson (p. 189) nor from those of the numerous authors who have reported the results of controlled and uncontrolled trials in many countries during the last five years. A few relevant details may be worth recording.

Fifteen patients were put on maintenance doses. They are still so maintained, some of them for longer than two years. There were no serious side-effects like diabetes, hypertension, or bleeding ulcer. Mooning and ankle oedema were frequent, but subsided after one or two weeks, as has been observed by others. In only two cases was it necessary to increase the maintenance dose permanently. Both were complicated by severe emphysema, and this disorder and the accompanying chronic bronchitis took their natural progressive course. In the other patients on maintenance doses (which varied from 25–150 mg./day) it was often necessary to increase the dose temporarily when the asthma became more severe after an intercurrent respiratory infection or after exposure to an allergen. In all such cases the daily dose was stepped up briskly to 150 or 200 mg. of cortisone and reduced gradually within the next 10 days until the previous maintenance dose was reached again. In all of them the asthma returned to its previous well-controlled degree of severity. Thirteen patients, who received the drug only temporarily in order to tide them over severe seasonal bouts of the disease, also returned to their previous moderate degree of chronic asthma after cortisone or A.C.T.H. had been gradually withdrawn.

In view of my own observations and those of many others, I must express disagreement with the somewhat gloomy view of your annotator, which is likely to discourage practitioners from the use of these most beneficial substances. We all know that cortisone and A.C.T.H. are only effective as long as they are given, and that they may have dangerous side-effects; so have many other drugs, including adrenaline, insulin, and chloramphenicol. We must try to avoid these dangers, but not by not using the drugs. Your annotator bases his view partly on the conclusions of Savidge and Brockbank,[1] who reported two deaths among their patients and collected nine other deaths from the literature. Their report makes it very likely that these two patients died not because they had too much but because they had too little cortisone. It was not continued or not suitably stepped up when the asthma temporarily increased in violence. Such violent bouts frequently occur in severe chronic asthma, and we must remember that, at present, cortisone is mostly used for severe cases in whom the risk of a fatal outcome is always present. The conclusion of Savidge and Brockbank "that the cortisone cannot be exonerated" (a conclusion echoed by your annotator) therefore seems unjustified. The authors contradict their conclusion themselves, for they suggest that in future higher doses should be given in such cases of deterioration.

Your further remark that trials with such a drug "must be blind" is not a happy one either. It may be interesting to stage a blind trial of cortisone against a placebo in order to determine statistically the percentage of placebo improvements. Such a trial would not be necessary to confirm the efficiency of cortisone, because its beneficial effect has already been generally confirmed and accepted—I shall not encroach on your space by quoting the 50 or so papers which have appeared on the subject since 1950. In view of this I wonder what is meant by the phrase, "*So far as this country is concerned* [my italics] the therapeutic value of cortisone and corticotrophin in asthma is still *sub judice*." I feel it is going a little too far to disregard the experience of reliable authors all over the world. The therapeutic value of cortisone has been established beyond doubt. We have still to learn many things about it, but this is no reason to discourage its use.

May I add a plea that leading articles and annotations be signed in the future? Their authors ought to shoulder their responsibility in public.—I am, etc.,

H. HERXHEIMER.

London, W.C.1.

REFERENCE

[1] *Lancet*, 1954, **2**, 889.

Human Nutrition and the Sophistication of Foods and Feeding Habits

SIR,—It is the duty of every commercial organization concerned with nutrition to ensure that their products not only conform to the relative applicable standards, but also to keep abreast of research in such a way that improvements may be introduced in any processing involved. Following Professor B. S. Platt's paper (*Journal*, January 22, p. 179), and since this department is concerned most particularly with the use of unsweetened evaporated milk in the field of infant feeding, we feel some reference to its protein value could be usefully made.

Hodson and Kreuger,[1] referring to evaporated milk samples obtained from six different areas, found a small and nutritionally insignificant loss of lysine in the heat processing of evaporated milk. They state: "When the variability of the assays is considered this is the only measurable indication of a loss of an essential amino-acid during the processing of evaporated or dried milk." More recently Hodson[2] reported the amino-acid content of evaporated milk on prolonged storage. In his summary of this work he stated: "Of the seventeen amino-acids studied, significant losses were found for only lysine (17%), histidine (17%), and arginine (11%) during five years' storage. During fifteen to seventeen months' storage, which is longer than the customary storage period, losses of these three amino-acids were not greater than 4% in any case."

We feel that perhaps even greater significance can be attached to the fact that the work of Hodson[3] in relation to yet further heating of the already heat-processed evaporated milk, utilizing the terminal heating method technique of preparing feeds, showed no further destruction of lysine. He stated: "Evaporated milk formulas, which were heat treated, either by low pressure method (100° C. for 15 minutes) or high pressure method (autoclaved at 110° C. for 10 minutes), showed no loss of the essential amino-acid, lysine." Further observations by Hodson refer to the darkening in colour when evaporated milk is stored for several years. He felt that because amino-acids contribute to the development of brown colour in food products, through their role in the Maillard browning reaction, a study of amino-acid loss during storage would be of interest. The study, therefore, embraced both essential and non-essential amino-acids, for which microbiological procedures had been devised. Having found the resultant loss of the seventeen amino-acids quoted above, Hodson[3] says: "If the amino-acids produce the brown colour in stored evaporated milk, through participation in the

Maillard reaction, then small amounts of lysine, histidine, and arginine must be very effective in producing the brown colour, inasmuch as only 2% of the total protein amino-acids would take part in the reaction during five years' storage."

In relation to curd and nitrogen storage, the investigation conducted at the Pennsylvania State College School of Agriculture by Professor Dizikes and F. J. Doan[4] shows that raw and pasteurized milk have unsatisfactory curd characteristics, since after three hours of digestion more than 50% of the nitrogen was found in curds failing to pass a 4-mesh screen. At this same stage—that is, three hours and 4-mesh—breast milk gave 0.0%, unsweetened evaporated milk 0.26%, and boiled milk 10.60%.

We trust this information will show our anxiety not to rest content with our product, and that we take into account as many factors as are currently known in relation to the use of a substitute food for infants when breast feeding is not possible.—I am, etc.,

London, E.C.4. R. H. WOODCOCK,
Manager,
Medical Department, General Milk Products Ltd.

REFERENCES

1 *Arch. Biochem.*, 1946, **10**, 55.
2 *Industr. Engng Chem.*, 1950, **42**, 694.
3 *J. Amer. diet. Ass.*, 1949, **25**, 119.
4 Pennsylvania State College School of Agriculture Bulletin No. 428, March 27, 1942.

Myxoedema After Thyrotoxicosis

SIR,—The case report by Drs. Russell Fraser and B. E. C. Nordin (*Journal*, January 29, p. 255) is interesting, but, although they mention Hashimoto's thyroiditis in the preamble, they do not describe the clinical state of the thyroid gland in their patient's myxoedema phase. There is some evidence that thyrotoxicosis may be present, and not uncommonly, early in Hashimoto's disease; is their case one of "struma lymphomatosa" in a male, which would be a rarity?—I am, etc.,

West Hartlepool. R. T. COOKE.

Prophylactic Thyroid Treatment in Cancer

SIR,—We disagree with the conclusion drawn by Dr. A. A. Loeser from the results given in the first paragraph of that part of his paper subheaded "Clinical Observations" (*Journal*, December 11, 1954, p. 1381). In the following paragraph the author states: "This fact shows that a lack of thyroid hormone in the body favours tumour development."

It is not stated whether or not the seven patients with cancer development had received thyroid hormone after thyroidectomy. Therefore, considering for the moment only the remaining 93 patients, we calculate that if 100 similar samples of thyroidectomized patients were examined, 18 would be expected to show differences of the observed amount (or greater), and in the observed direction, on the basis of random sampling. The chances against such an occurrence are 4.4 to 1. Therefore the observed difference of tumour development between the group which had received thyroid hormone and that which had not has very low statistical significance. If the seven patients with cancer development are supposed not to have received thyroid hormone (which would be favourable to the conclusion drawn in the paper), and are included in the analysis, the chances are 9 to 1 against the observation being the result of chance. This result is one-half the chance which is considered by many to indicate "satisfactory significance" in a biological experiment, and falls far short of that which would permit an almost certain conclusion to be drawn.

If Dr. Loeser's conclusion is correct, it might be shown to be so statistically with greater certainty if a larger number of patients were included in the group having received thyroid hormone. We note, also, that reference is made on two occasions to cancer incidence in the "average population" for purposes of comparison, but we can find no mention of the magnitude of this incidence.—We are, etc.,

J. J. HANDLER.
Oxford. D. G. WYATT.

Medical Aspects of Amateur Boxing

SIR,—We would like to answer some of the points raised by Dr. J. C. Laurie in his letter (*Journal*, January 22, p. 227) concerning medical aspects of amateur boxing. We cannot accept the pathological concept that concussion invariably produces oedema of the brain, and, while admitting that full recovery from a knock-out may not be instantaneous, we believe that lasting brain damage is unlikely to occur in amateur boxers if adequate medical supervision is enforced. In London a boy who is knocked out has to stay off boxing for at least a month, and *all* boys are examined before *all* contests. A bout is stopped immediately a contestant receives a cut, whereas in professional boxing the bout may be allowed to continue. A solar plexus blow does not cause unconsciousness, but a transient muscular weakness of the legs is produced and the boxer rapidly recovers, with no after-effects. We made no reference to it in our article (*Journal*, December 25, 1954, p. 1524), because it has never been a serious medical aspect of amateur boxing and is not related to the problem of head injury.

We are amazed at the conditions described by Dr. Laurie under which amateur boxing is alleged to be conducted in Scotland. If these facts are true, the sport must be in a very primitive state. We are also surprised that Dr. Laurie, who is shocked by the lack of medical control, continues to act as medical officer, thus condoning a state of affairs of which he justifiably disapproves. We can only suggest that the Scottish Amateur Boxing Association should be given the opportunity to refute these allegations.—We are, etc.,

London, W.1. J. L. BLONSTEIN.
London, W.12. EDWIN CLARKE.

Trichomonal Vaginitis

SIR,—We are grateful to Mr. Aleck Bourne for his letter (*Journal*, January 22, p. 226) drawing attention once again to the difficulties of treating and curing trichomonal vaginitis. We agree with many of his observations, but were particularly interested in his remarks about placing pessaries in the vaginal fornices under direct vision through a speculum. We have treated a few cases of trichomonal vaginitis by filling the vagina with a liquid preparation of amido-nitrothiazole. The patient was placed in the lithotomy position and the vaginal walls were stretched with a bivalved Cusco speculum. The fluid was injected with a Ritchie's bladder syringe and was retained in the vagina for twenty minutes. The fluid was then removed and a paste containing amido-nitrothiazole liberally applied to the vaginal walls, care being taken to see that the fornices were well filled. A plug of cotton wool was then inserted into the vagina and the patient was sent home and reported the following day for examination. It was hoped that such treatment would be effective without the necessity of relying upon the patient to insert pessaries herself. Unfortunately all five patients so treated relapsed, or were perhaps reinfected, shortly afterwards. Details of this work will be published soon in a forthcoming number of the *British Journal of Venereal Diseases*.

Our primary object in describing our work (*Journal*, January 8, p. 78) with amido-nitrothiazole was not merely to add yet another trichomonacidal drug to the large list already available, but to introduce a substance which was found to be almost as effective as acetarsol, but which was a non-arsenical and did not carry the risk of arsenical sensitization. We have found that in the long-term treatment of resistant cases or chronic relapsing cases it is useful to have an alternative drug available. Perhaps the most important conclusion to be drawn from our results and Mr. Bourne's comments upon them, as well as from most other recent work, is that the problem has been much neglected and requires more investigation if this widespread and distressing condition is to be controlled.—We are, etc.,

R. D. CATTERALL.
London, E.1. MARY WILLIAMSON.

Tuberculous Patients in General Hospitals

SIR,—Any prospective entrant to the nursing profession who has read or heard of the recent correspondence in the *Journal* on the vexed question of tuberculous patients in general hospitals would, in my opinion, be stout-hearted indeed if her prospective entry became fact. Against this, might I submit that an intelligent girl presented with a factual and up-to-date account of tuberculosis nursing might not forgo a nursing career simply because a part of her training period was to be spent in a tuberculosis hospital, and later—who knows—she might even voluntarily join the staff of a chest hospital.

It has been well said that one of the places where one is least likely to contract tuberculosis is in a chest hospital—and this was said at a time when the incidence of "human wrecks" in tuberculosis wards was far higher than to-day. Evidence from Papworth Settlement substantiates this. The "overall infectivity" of a tuberculosis unit in a chemotherapeutic age is surely wellnigh negligible, when compared with bygone days. Even Dr. J. F. Brailsford's "unbiased layman" (*Journal*, January 15, p. 164) would probably agree with this—if he knew the facts.

The dread of tuberculosis was once well founded. But can it be that an almost superstitious fear is still infiltrating professional and lay ranks alike? Constant contemplation of the fearful in many instances promotes a *laissez faire* attitude. One is reminded of the dog on the thistle, in considerable pain but too lazy to get off. Let us have a forceful, up-to-date, and factual propaganda with regard to tuberculosis nursing, and even the fondest parent—so often the chief barrier to the prospective student nurse—would see things far less through a glass darkly. There would then perhaps be no need even to consider Dr. Brailsford's possible solution of more and more domiciliary treatment of tuberculosis, which bristles with pitfalls and difficulties, some of which, in many instances, can be quite insuperable.—I am, etc.,

Stornoway. EWEN A. CAMERON.

SIR,—The case for and against the use of wards in general hospitals for the treatment of patients with pulmonary tuberculosis has been argued for some weeks now since you published Dr. A. B. Cowan's letter (*Journal*, November 20, 1954, p. 1227). Such a scheme may be an innovation for Glasgow; it is certainly not so for London.

But is this controversy wholly necessary? The Royal National Hospital for Diseases of the Chest, founded, equipped, and staffed for the treatment of tuberculosis by all methods, ancient and modern, medical and surgical, has been unable to find patients to fill all its beds since June, 1954; and for several weeks now has had no fewer than 70 beds unoccupied—more than a quarter of its total. (This is in no way due to shortage of staff. Only once in our history has part of one ward been closed for lack of nurses; and, *pace* Dr. J. F. Brailsford (*Journal*, January 15, p. 164), there has more than once since the war been a waiting-list for our nursing staff.) Such a situation is certainly frustrating for the staff and presumably uneconomic for the service. No doubt it will be remedied when the necessary committees have had time to give it the necessary consideration, and one may hope that one step will be the liberation of some of the wards in general hospitals in London, which are so badly needed for other purposes. I do not refer to the wards of which Dr. P. Stradling (*Journal*, December 18, 1954, p. 1483) writes—one cannot but agree with him that continuity of treatment is an overriding advantage—but there are others where the chest physician does not attend his patients; indeed, until recently it was no uncommon thing for a patient to have been in three, and even four, different London hospitals before reaching here.

Meanwhile the Regional Board has, happily, permitted the hospital to accept patients from all parts of the country, as it always had the honour of doing before July, 1948. It is very much hoped that use will be made of this opportunity. One realizes that many would not wish to come from, say, the north or the midlands to the far south. But there will always be some who are glad to do so; others who may actually benefit by being at a distance from their daily troubles; and yet others who will gladly submit to the inconveniences in order to save delay. It would be a great pity if administrative difficulties were put in the way of patients (or their physicians) willing to go to a distance for their treatment. Transport is truly expensive; but less so than the undebited cost of needless prolongation of treatment.

It is not suggested that these 70 beds are the answer by themselves to our problems. But they can help and surely should be allowed to do so. One solution to present difficulties is to see that we have a national and not a regional health service.—I am, etc.,

Ventnor, I. of W. E. F. LAIDLAW.

Treatment Abroad of Tuberculous Children

SIR,—A recent news item in a national daily paper[1] draws attention to treatment in Denmark of children "from industrial towns in all parts of Britain where the hospitals are overcrowded." It would be interesting to know which of our towns are concerned and why in any event treatment has to be sought outside the country. My own hospital treats tuberculous children from all over London and the home counties. We have no waiting-list and no overcrowding. On the contrary, at the present time there are many empty staffed beds waiting for patients.—I am, etc.,

Brentwood, Essex. F. J. BENTLEY.

REFERENCE

[1] *News Chronicle*, January 20, 1955.

Fluoridation of Water Supplies

SIR,—Much has been written on the value of fluorine in the prevention of dental caries. A certain amount has also been written on the role of fluorine in the causation of dental caries. In *Hygiene*,[1] under "Dental Fluorosis": "This dystrophy of the teeth of children begins with a dark mottling of the enamel which may go on to permanent blackening or even disintegration of the dental substance... the active agent of the mischief is fluorine . . one part per million of the element enables a water to start the process of destruction, which, it should be noted, is almost exclusively limited to the permanent teeth." Dr. Eugene Payne, in "Islands of Immunity,"[2] writes: "In some countries a number of communities are artificially fluorinating their water supplies to prevent tooth decay. In Brazil, in areas where fluorine in the water is absent, I found communities with sensationally good teeth. The incidence was lower than any reported in the fluorine-using towns. We need to investigate the reason why."

In small amounts fluorine appears to cause calcium fixation and in larger amounts calcium deprivation. Chronic fluorism may thus present as osteosclerosis, osteomalacia, and calcification of ligamentous attachments, whilst acute excess may be manifested by persistent cough, dyspnoea, sickness, constipation or obstipation, effects reminiscent of the other 'flu. In its affinity for calcium its action recalls that of lead, and it is of interest that both substances are again associated in the production of high octane aviation fuel as hydrogen fluoride and lead tetra-ethyl. In addition to its violent chemical affinities, fluorine is highly reactive to electro-magnetic radiations, a property employed, for example, in *x*-radiography, television, and atomic physics. One is fascinated by the prospect of "selected" communities subsequently exhibiting fluorescence under the influence of atomic radiation. Seriously, however, it does seem a matter calling for further trials on a more limited scale, and in the meantime those of us who exhibit dental caries may find consolation in the knowledge that dental excellence is pre-eminently the attribute of the negro and the American.—I am, etc.,

Uffculme, Devon. F. MURRAY.

REFERENCES

[1] Currie, J. R., and Mearns, A. G. (1948). *Hygiene*. Edinburgh.
[2] *Reader's Digest*, December, 1953.

Differential Diagnosis of Coma

SIR,—It is with regret that I must point out an omission in the otherwise excellent article by Dr. M. J. Parsonage (*Journal*, January 22, p. 217). In discussing the differential diagnosis of coma no reference is made to the possibility of this being caused by cerebral malaria. The omission emphasizes the fact that this form of malaria is commonly overlooked, and this probably in part results from defects in the teaching of medical students. In many schools students are not made sufficiently aware of the emergencies which, even in this country, may result from tropical illness.

In these days of increasing air travel it is possible for many varieties of exogenous disease to be contracted abroad but not to become manifest until the patient has returned to a temperate region and, in spite of being advised to do so, patients or their relatives when reporting illness to a doctor commonly do not tell him when they have recently been abroad. The previous movements of the patient should be ascertained *by the doctor* as a routine in every case in which they are not known, and when the patient has been to the Tropics the possibility of tropical illness should be considered whenever the diagnosis is in doubt.—I am, etc.,

London, N.W.1. A. W. WOODRUFF.

SIR,—In the refresher course on the differential diagnosis of coma (*Journal*, January 22, p. 217) I was horrified to see that there was no mention of malaria

In malarious countries, where many thousands of your readers reside, this omission will only have the effect of lowering the prestige of your excellent *Journal*, since nearly all the readers will know that the first thing one thinks about when a comatose child (especially) is brought into the dispensary is malaria, and that when this has been satisfactorily excluded it will be time to embark on Dr. Parsonage's "orderly approach."

However, in Great Britain the effect of this omission may be much more serious. In these days of easy and rapid air travel it is by no means uncommon for the first clinical evidence of malaria to appear in this country. For example, schoolchildren often spend part of their holidays with their parents in the Tropics. Not all are given prophylactic antimalarials, and, even if they were, there are certain strains of *Plasmodium falciparum* that are resistant to some of the newer antimalarials; one of these children might well develop an attack of cerebral malaria at school. In his "orderly approach" Dr. Parsonage would be well advised to include an inquiry as to the recent movements of the patient, since there is no medical emergency in which treatment is so dramatically rewarding as it may be in cerebral malaria.—I am, etc.,

London, W.1. L. EVERARD NAPIER.

The Princess Louise Children's Hospital

SIR,—The Goodenough Committee recommended[1] that a teaching hospital should provide for paediatric teaching not more than 10% of its beds; because in the St. Mary's Hospital group the children's beds amount to 19.2%, its board of governors are considering achieving a reduction to 10% by converting to adult use the Princess Louise Children's Hospital, a small hospital which has served the children of the Royal Borough of Kensington and its neighbours since 1840.

There are at present 9,690 beds for undergraduate teaching in London, of which 9.3% (909) are beds for children. If the St. Mary's group has 19.2% of its beds devoted to children, then it is clear that some other teaching groups have much less than the 10% recommended by the Goodenough Committee; so that although the conversion of this small hospital to adult use will benefit St. Mary's to the extent of relieving its board of governors of an arithmetical problem, it will benefit no one else, and the recommendations of the Goodenough Committee in this matter as they relate to the London teaching hospitals as a whole will be further from attainment than ever before.

The "Co-ordinating Committee" responsible for making this recommendation seeks to show that the waiting-lists of the children's department of St. Mary's Hospital reflect a fall in demand for children's beds throughout the country, and it presents figures—not fully quoted in your note (*Journal*, January 29, p. 299)—to support this view. If we examine these figures, we find that they do not in fact do so. The Committee says that the children's waiting-list has fallen from 539 in 1952 to 235 at the present time, of which 159 are ear, nose, and throat cases. What it does not disclose is that in 1952 the proportion of ear, nose, and throat cases was 435, so that the fall in the numbers on the general medical and surgical waiting-lists has been from 104 to 76, a reduction which few will regard as being significant of the trend it is sought to demonstrate. In fact, the reduction of the numbers on the children's waiting-lists reflects not a reduction in demand for the services of the hospital, but the results of a drive on the part of the staff of the ear, nose, and throat departments to reduce the tonsil and adenoid lists.

It is right that the governors of St. Mary's Hospital should show due concern over the training of their students, but it is a little unfortunate that this should seem to overshadow their concern for the welfare of their patients in this thickly populated and rather inaccessible part of London. In the statement they have issued this latter aspect of the question receives no practical consideration at all.—I am, etc.,

London, W.10. JOHN BATE.

REFERENCE

[1] *Report of the Interdepartmental Committee on Medical Schools*, 1944. H.M.S.O., London.

Unwrapping the "Journal"

SIR,—A year ago you published a discussion on the wrapping of the *Journal*. May I, as the initiator of the correspondence (*Journal*, December 12, 1953, p. 1326) and after controlled observation and experiment, pay a tribute to the efficacy of the method advocated by Dr. G. M. Grant, of Dundee (*Journal*, December 26, 1953, p. 1432)? That is, gripping the wrapped *Journal* in the supinated left hand, so creating a trough; inserting a finger of the right hand into the trough and pushing it along. Your part in ensuring the success of this simple procedure is to see that the journal is loosely and *not tightly* rolled before postage.—I am, etc.,

Cross-in-Hand, Sussex. H. LYNDHURST DUKE.

POINTS FROM LETTERS

Crying in Infants and Children

Dr. E. BARNES (Manchester) writes: I once was called to a perfectly good baby of 3 months. The mother complained that when she laid him down he cried; on picking him up, he crowed happily. After four or five of these trials, she sent for me. I asked her to strip him, and I found in his singlet a short bristle of a tooth-brush perpendicular to the material. Removal put matters right.

Disk Lesions and Low Backache

Dr. A. LASK (London, W.13) writes: Mr. John Charnley's stimulating letter (*Journal*, January 15, p 163) should provoke much comment. . . . I refer, of course, to his therapy of reassurance. The emotionally charged tone of his letter, obviously sincere, suggests that Mr. Charnley just does not see these patients as sick human beings (psychoneurotics) at all, but only as sound non-pathological spinal columns with bodies attached. He does not seem to recognize that there is a real problem here. What is the process by which an individual with no organic lesion comes to suffer so much discomfort or dis-ease that he continues to appeal for help in relief of his pain? What is the best method of helping these neurotics? The psychotherapist should offer the soundest opinion here. The orthopaedic surgeon has no special authority, and no justification for acting as the "final court of appeal." Let him refer these patients to the right quarter.

Obituary

J. HARDIE NEIL, C.B.E., D.S.O., F.R.A.C.S., F.A.C.S.

Mr. J. Hardie Neil, consulting aural surgeon to Auckland Hospital, New Zealand, died at Auckland on January 28 at the age of 79.

James Hardie Neil was born at Dunedin, New Zealand, on February 27, 1875. From Otago Boys High School he entered Otago University as a medical student, and, after graduating M.B., Ch.B. in 1898, held the appointment of resident surgeon at Auckland Hospital. Soon afterwards he went as a surgeon captain with the 4th New Zealand Mounted Rifles to serve in the South African War in 1900–1, being awarded the Queen's medal with four clasps. After the war he came to England and took the London Conjoint Diploma in 1902.

Returning to New Zealand, Hardie Neil was appointed ear, nose, and throat surgeon to Auckland Hospital in 1903, and he held the post for the long period of 45 years until 1948, when he was appointed consulting surgeon. For many years he was also aural surgeon to the Mater Hospital at Auckland. During the first world war he served as a lieutenant-colonel in the New Zealand Medical Corps, and was in command of No. 3 Field Ambulance with the New Zealand Rifle Brigade from 1915 to 1918. For his services he was awarded the D.S.O. and the Belgian Croix de Guerre in 1918, and was three times mentioned in dispatches. From 1924 to 1929 he was A.D.M.S. of the New Zealand Northern Command. During the last war he was deputy director of Auckland medical boards from 1940 to 1946. In 1947 he was appointed C.B.E.

A member of the British Medical Association since 1899, he was chairman of the Auckland Division in 1923–4. In 1921 he was elected the first president of the newly formed Auckland Clinical Society. He was also president of the otolaryngological section of the New Zealand Medical Conference in 1924 and of the Pan-Pacific Surgical Association in 1939. His presidency of the New Zealand League for the Hard of Hearing was no titular office, for he conducted an energetic campaign against unscrupulous salesmen and misleading advertisements of commercial hearing-aids, always with the aim of alleviating the distress of the afflicted. In recent years he had devoted much time and thought to the nomenclature of the anatomy of the bronchial tree, a subject neglected until just before the second world war. With Drs. W. Gilmour and F. J. Gwynne, Hardie Neil was the author of an authoritative article printed in this *Journal* in 1939. This paper, the result of long and painstaking work, was followed by another presenting in greater detail the results of their study. The second communication was read before the Auckland Clinical Society in 1945 and was printed in the *New Zealand Medical Journal* in the following year. He also wrote, jointly with Dr. Gilmour, an article on bronchopulmonary segments of the lung and their terminology, which was published in the *British Medical Journal* in 1949. Other writings from his pen included a small book on *Field Ambulance Organization and Administration*, published in 1918, and *Ear, Nose, and Throat Nursing*, which ran to several editions.

Hardie Neil was elected a Foundation Fellow of the Royal Australasian College of Surgeons in 1927. He was also a Fellow of the American College of Surgeons. He married Miss Mary E. Coates in 1904 and had two sons and four daughters.

Sir FRANCIS TREHERNE, K.C.M.G., F.R.C.S.Ed.

Major-General Sir Francis Treherne, one of the oldest members of the Army Medical Service, died at his home at Woodbridge, Suffolk, on January 30.

Francis Harper Treherne was born in 1858, the son of an audit clerk at Somerset House. He was educated at Godolphin School and received his medical training at St. Bartholomew's Hospital, qualifying in medicine in 1881. Three years later he took the F.R.C.S.Ed. and in 1887 the D.P.H. of Cambridge. He immediately adopted the Army as a career. In 1884 he was serving with the Egyptian Expeditionary Force and in the following year in the Sudan Expedition. In each case his services were recognized by mention in dispatches and by decorations. The year 1893 saw him in India, now a major in what, a few years later, became the R.A.M.C., and for five years he was surgeon to the Commander-in-Chief.

Then came the South African War, during the whole of which he served with the British forces and won campaign medals and further mention in dispatches. Later on, in 1908, he saw service on the North-west Frontier of India. In 1912 he was honorary surgeon to the Viceroy (Lord Hardinge of Penshurst), and for three years Assistant Director of Medical Services in India. When the first world war broke out in 1914 he was Deputy Director of Medical Services of the Indian Corps which formed part of the British Expeditionary Force, and during the later years of the war he served as Director of Medical Services of the Third Army. His services in France in 1914–16 received mention three times in dispatches, and afterwards he was sent to Mesopotamia and was in the actions at Kut and Diala and at the capture of Bagdad. Later he was Deputy Director of Medical Services in the London District and inspector of hospitals in the Southern Command. His last period of service was as Inspector of Medical Services, stationed at the War Office. Appointed C.M.G. in 1915 and K.C.M.G. in 1917, he retired in 1919 with the rank of major-general and went to live at Woodbridge, in Suffolk. He married twice. One of his sons by his first marriage, Captain Claude Treherne, R.A.M.C., died of wounds in the first world war.

G. PRATT YULE, M.D., F.R.C.P.Ed.

Dr. G. Pratt Yule, formerly medical officer of health for Fife County, died in the Adamson Cottage Hospital, Cupar, on January 6. He was 81 years of age.

George Pratt Yule was born on July 30, 1873, and was educated at George Watson's College and at Edinburgh University, where he graduated M.B., C.M. in 1894. Two years later he obtained the B.Sc. in public health and in 1899 proceeded to the M.D. He became a Member of the Royal College of Physicians of Edinburgh in 1900 and was elected a Fellow in 1905.

After graduation he worked in the pathological laboratories at Larbert Institution and later at the Crichton Royal Institution, Dumfries. He was then appointed assistant to Dr. (later Sir) Leslie Mackenzie, medical officer of health, Leith. Subsequently he became resident medical officer at the Edinburgh City Fever Hospital and still later went to the Corporation Fever Hospital, Manchester. In 1900 he volunteered for service in

the South African War and was appointed second in command of the Edinburgh and East of Scotland Hospital, stationed at Norval's Point, on the Orange River. He was given this post because of his specialized knowledge of fevers, particularly typhoid fever, since typhoid fever was at that time rife among the troops. Dr. Pratt Yule remained in Africa to work in a military hospital at Bloemfontein until he was appointed health officer for the area. After a brief return to this country he was recalled by Lord Milner to serve as principal medical officer for the Orange River Colony, a post which he held until he left South Africa in 1912. The position he held was a responsible one and he carried out his duties with vigour and foresight. He assisted in the introduction of legislation covering a wide field of public health practice and medical service and thereby established for the first time in the State an organized medical service.

In 1912, soon after his return to Britain, he was appointed medical officer of health for Fife, a position he held until his retirement in 1938. He became an examiner in public health in Edinburgh University, and in Fife played a big part in the intensive work of reorganization which followed the introduction of the Local Government (Scotland) Act, 1929. He was successful in bringing into being a unified maternal, child health, and school health service. The first health visitor was appointed in Fife in 1909, and Dr. Pratt Yule, throughout his whole period of office, fostered and expanded this form of domiciliary service. He was instrumental in securing the erection of Glenlomond Sanatorium. The foresight and determination with which he utilized the increased powers devolving upon local authorities for the promotion of the public health resulted in his laying the solid foundation on which the health services of Fife stand to-day.

Dr. Pratt Yule is survived by a widow, a son, Dr. Alastair Pratt Yule, who is in practice in Cumberland, and two daughters, one of whom, Mrs. Lawrence, was appointed professor of psychology in the University of Natal in 1953.

ROBERT GRIEVE, M.D., F.R.C.S.Ed.

Mr. Robert Grieve, honorary consultant surgeon to the Hull Royal Infirmary and the Victoria Hospital for Sick Children, Hull, died suddenly at his home at Hull on December 30, 1954. He was 83 years of age and had been in active practice over a period of sixty years.

Born in London on November 22, 1871, the son of Dr. Robert Grieve, who at one time was Surgeon-General of British Guiana, Robert Grieve, junior, came of a family of Scottish lowlanders with a long medical tradition. He received his early education at Bedford, later studying medicine at Edinburgh University and graduating M.B., C.M. in 1894. Three years later he proceeded to the M.D., with commendation, and in 1900 he was elected F.R.C.S.Ed. In the same year, after having held several appointments, he became honorary assistant surgeon to the Hull Royal Infirmary. In 1918 he was elected full surgeon, a post which he held until reaching the age of retirement in 1932. During his years on the full staff he became senior surgeon, chairman of the medical committee, and a member of the board of management. On retiring from the infirmary staff he continued to serve as honorary surgeon at the Victoria Hospital for Sick Children until the inception of the National Health Service in 1948. During the second world war, although then well on in years, he never failed to respond to the many calls on his services for the treatment of air-raid casualties and other emergencies.

Throughout a busy surgical life Robert Grieve remained in general practice, the last of a generation of general-practitioner surgeons who rendered such outstanding service to voluntary hospitals in the locality. On relinquishing surgical work he continued in his general practice and was visiting patients on the day he died. A member of the British Medical Association for 57 years, he was chairman of the East Yorkshire Division in 1928–9. He was also a member and a past-president of the Hull Medical Society, and only recently he had been elected an honorary member of the society as a mark of the affection and esteem in which he was held by his colleagues. Robert Grieve was a man of quiet and kindly disposition, which endeared him to all. He had a pawky sense of humour and a fund of medical anecdotes. A skilful and versatile surgeon, he devoted his whole life to his profession, earning the gratitude of his colleagues and countless patients. As befitted his character, he enjoyed the quieter pursuits, reading, his garden, and the company of his friends. He was a bachelor, and is survived by a brother and two sisters, to whom our sympathy is extended.—J. N. Y.

Sir EDWARD MELLANBY, G.B.E., K.C.B.
M.D., F.R.C.P., F.R.S.

The obituary notice of Sir Edward Mellanby was published in last week's *Journal*. We have since received the following appreciations.

Sir ARTHUR MACNALTY writes: Edward Mellanby and I were friends for many years. When I became Chief Medical Officer of the Ministry of Health in 1935, one of my chief aims was to bring the work of the Medical Research Council into closer relation with that of the Ministry. Mellanby supported me in this endeavour. He became a member of the Minister's Medical Advisory Committee, and he and I met at least once a week to discuss problems of medical research and their practical application. He and Sir John Ledingham helped me to get diphtheria immunization more generally applied; this work has reaped a golden harvest in combating a disease so fatal to child life and especially to the schoolchild.

In the early years of the second world war we planned the Emergency Public Health Laboratory Service together, for which the Medical Research Council took practical responsibility. Its value in aiding national health during the war and subsequently cannot be overestimated. When I left Whitehall to become editor-in-chief of the official medical history of the war, Mellanby joined our editorial board, and by his nomination of Dr. F. H. K. Green and Sir Gordon Covell enabled the war work of the Medical Research Council to be adequately recorded in a volume of the *History*.

These were our official relations, but they were facilitated and made pleasant by our friendship. Sometimes we disagreed on a particular policy, but we always agreed to differ. He was ever young in mind and body. Through his endeavours in peace and war he lived to see the work of the Medical Research Council greatly extended on the foundations so ably laid by Sir Walter Fletcher. Mellanby's own work on rickets has blessed mankind. He was fortunate in his life and work, and not least in the collaboration of his distinguished wife, Lady Mellanby, to whom our sympathy goes out to-day.

Professor A. E. BARNES writes: When Mellanby became the first professor of pharmacology at Sheffield an attempt had been made to arrange facilities for him for clinical work in his own beds as a physician at the Royal Infirmary as well as laboratory work in the pharmacological department at the University. In a few months he had succeeded

in adding the field laboratory at Lodge Moor, where very careful nutritional work was done on dogs. It was a tremendous job, but he and his wife worked for all they were worth and did their famous researches on rickets, including May Mellanby's work on the nutritional problems of dentition. Although it was not until many years afterwards, I think it is true that it was there that they first met with the toxic results of agene. The final incrimination of agene as the active factor in the causation of canine hysteria was a masterpiece of criminal detection aided by their scrupulous experimental methods. His conclusions were attacked with zeal by able and well-equipped workers, only to elicit confirmation just as had been the case years before when he announced the presence of an anti-calcification factor in oatmeal.

As a teacher Mellanby was superb. He aroused the enthusiasm of his students and of his colleagues. The general practitioners of Sheffield were enlisted in the enthusiasm, and the panel committee gave a donation (from a voluntary levy) of about £2,000 to the department. He was interested in the metabolism of alcohol, especially in diabetics, at a time when the Allen pre-insulin methods were our only resort and every calorie counted. One patient who submitted himself to venepuncture in these experiments was also many months later his first insulin patient. Rarely has a physiologist had such an opportunity of repaying one of his human "guinea-pigs," for he won only by a very short head. As a member of the staff at the Royal Infirmary he was a general favourite with all ranks. He was most stimulating, not to say provoking, and one member a year or two after his departure to London said at lunch one day, "Are we not a dull crowd since Mellanby left."

Some time ago he and Lady Mellanby went to a dinner at Sheffield held by the newly formed Medical Students' Association, and they had a great reception. In a letter he summed it up, "It was a jolly evening except for my speech." Of his work as secretary of the Medical Research Council others have written. After his retirement he again found more time for research and was very busy indeed. Tissue culture (in collaboration with Honor Fell) occupied a lot of his attention. In a recent letter he states: "Lately we have been using radioactive isotopes and making autoradiographs in the tissue culture experiments, and it has been most enlightening. These new techniques, including chromatography, have transformed the study of biological problems, and I am only sorry that I was born too soon to get my teeth into them." These were, however only a part of his activities during his "retirement." As he would have wished, he died at work, though not actually in the laboratory. On holiday he was a delightful big boy, always good company. His death ends not only a happy marriage but a long and useful partnership in the service of medical science. The heartfelt sympathy of innumerable friends will go out to Lady Mellanby.

Dr. M. N. GHOSH writes: I find no reference in your obituary notice of Sir Edward Mellanby to the significant part he played in establishing the Central Drug Research Institute at Lucknow—one of the 11 national laboratories that have been started in India since her independence. This Drug Research Institute, the primary function of which is to investigate the potentialities of the indigenous drugs of India, was formally opened in 1951 by Mr. Nehru, the prime minister, and Sir Edward Mellanby was its first director, from November, 1950, to February, 1951. During his stay in India at that time Sir Edward also presided over the eleventh session of the All-India Pharmaceutical Conference, which was held at Bangalore along with the Indian Science Congress.

C. H. HAMPSHIRE, C.M.G., M.B., Ph.C.

Dr. F. H. K. GREEN, Principal Medical Officer of the Medical Research Council, writes: I do not think that any of the obituary notices of Dr. Hampshire so far published have mentioned the important work he did during the second world war as secretary of the Medical Research Council's Therapeutic Requirements Committee. This committee was appointed at the request of the Ministry of Health, and by arrangement with the Ministry of Agriculture and other Government departments, to advise the wartime controllers of the importation and manufacture of drugs as to which drugs were vitally necessary and must be supplied at all costs, and which were less important; it informed the medical and veterinary professions and those responsible for the formularies, indents, and quotas, as to which medicaments were scarce and must be used economically; and it dealt with the manifold and difficult problems which inevitably arise when restriction has to be practised and indicated where exceptions should be made to avoid hardship. For all these functions Dr. Hampshire's unique experience made him the ideal secretary of the committee, and he discharged the duties with tact and skill.

I personally shall always be grateful to Dr. Hampshire for the help he gave to me and to my colleague, Dr. F. Hawking, when we were editing the two editions of the Medical Research Council War Memorandum No. 10, *The Medical Use of Sulphonamides*. We frequently went to him for advice on points within his wide field of expert knowledge, and never in vain.

R. J. WILLAN, C.B.E., M.V.O., M.S., F.R.C.S.

R. A. writes: The passing of R. J. Willan is indeed a sad blow to the profession and a great sorrow to his friends and colleagues. I had the privilege of serving under him in the first world war and of knowing him more intimately since the last war. One remembers with affection and gratitude the care and the time he devoted to the guidance and the instruction of surgeon probationers. Professor Willan was a man admired alike for his great personal charm and for his distinguished professional career. He was at all times courteous and modest, yet ready and willing to advise from his superior and expert knowledge. Of upright principles, he was kindness itself, understanding and sympathetic, and would do all in his power—even when physically unfit—to help the sick. As a patient he was co-operative and courageous in his painful malady, and always grateful for anything one could do for him. Professor Willan will be sadly missed by all who knew him.

H. A. C. writes: I should like to pay my small tribute to the memory of Surgeon Rear-Admiral Willan. I first met him in 1945 when he used to visit the R.N. Hospital, Port Edgar, in his capacity as consulting surgeon to the Navy in Scotland. It was his custom to leave after lunch in his car to travel back to Newcastle; but one day he altered his routine and spent the night in the medical mess. I shall always remember that evening after dinner, how he entertained us all with his stories and kept us up to a late hour thoroughly enjoying ourselves. Although I have never seen him again since that night, I have always had a soft spot in my heart for him. He must indeed have been a very good messmate in his younger days while serving at sea in the R.N.V.R. during the first world war. I am sure that all R.N. medical officers who met him held him in high esteem and liked him, for he was indeed a very likeable man.

HENRI GOUGEROT, M.D.

Dr. Henri Gougerot, the eminent French dermatologist, died in Paris on January 15, aged 73. He was born at St. Ouen-sur-Seine on July 2, 1881, and after a medical education in Paris he qualified in 1908. Two years later he became professeur agrégé in the faculty of medicine and a hospital physician. He served in the French Army during the war of 1914–18, being awarded the Croix de Guerre. In 1928 he was appointed to the chair of clinical dermatology and syphilology at Paris University and became chief physician at the Hôpital St. Louis, posts which he held at the time of his death.

Gougerot made a number of important contributions to the literature of his subject; in 1909 he first described

hemisporosis and, with de Beurmann, gave the first complete account of sporotrichosis (de Beurmann–Gougerot disease) in 1912. He wrote also on sarcoidosis, lupus, cutaneous papillomatosis, and the prevention of venereal diseases, edited the *Archives dermato-syphiligraphiques de la clinique de l'Hôpital Saint-Louis*, and was a co-editor with Darier, Sabouraud, and others of the *Nouvelle Pratique Dermatologique* (published in eight volumes in 1936). He was president of the Société de Dermatologie et Syphiligraphie in 1934, and an honorary president of the ninth international congress of dermatology and syphilology, Budapest, 1935. He also presided over a number of national organizations concerned with social hygiene.

JAMES WHILLIS, M.D., M.S., F.R.C.S.

T. P. K. writes: I crave space for a small tribute to Professor James Whillis (whose obituary was published in last week's *Journal*) from that group of consultants, registrars, and visitors who meet at Stoke Mandeville Hospital every Monday to discuss their problems of construction, reconstruction, and repair. James Whillis visited us once a month, and only illness or the pressing call of one of his other "extramural" activities was allowed to cause us the disappointment produced by a cancellation of the visit. Not everyone will know that Stoke Mandeville Hospital, Aylesbury, is roughly 40 miles north-west of London, and that Whillis lived at Seal, near Sevenoaks, some 30 miles south of the Metropolis. It was a measure of the value he placed on these visits that he was prepared to arrive at the hospital mid-morning and not leave to travel home by train via London until night, with the expectation of reaching home about midnight. These visits were to us a means of keeping us on the right lines anatomically and functionally, and to him a link with the clinical applications of his specialty, and, indeed, with clinical matters in general. Our apologies to his wife for this imposition were always considered unnecessary, because she knew how much her husband enjoyed these visits. He would watch operations until lunch and spend the whole afternoon in the clinic, where out-patients and in-patients were freely and fully discussed. To these discussions he always contributed much sage advice, and his presence was as invigorating as a breath of fresh air. If time allowed he would round off the session with a "lecturette", on some anatomical subject of our choice before we carried him off to dine with us in Aylesbury, hear one of those yarns he told so well, and reluctantly see him to his train.

Everyone who met Whillis was fascinated by his boyish (almost puckish) outlook; all who knew him developed for him a deeply affectionate regard. He had many friends and surely no enemies. We shall remember him as the man with the articulated finger bones in his pocket—always ready to demonstrate the disturbances of function so commonly seen in the burnt finger—and as that rare teacher who could make anatomy live and embryology understandable. We shall keep on remembering (and missing) him in a thousand and one ways, but most of all for his warm and loyal friendship.

The winter number of the *Army Medical Services Magazine*, published last month, includes a reproduction of a photograph of the funeral procession of the late Major (temporary Lieutenant-Colonel) W. R. W. WEST-WATSON, R.A.M.C., who lost his life in an aeroplane disaster in Alaska on February 5 last year, and was buried in the Kermit-Roosevelt cemetery in Alaska. His father was the late Dr. W. N. West-Watson, who died in 1949, and who was a tower of strength to the Bradford Division of the British Medical Association as its secretary for many years and later its chairman; he was also local general secretary of the Bradford Annual Meeting of the Association in 1924. William Ronald West West-Watson was born on April 6, 1914, and was educated at Aldenham School and at Leeds University, taking the London degrees of M.B., B.S. in 1938. After graduation he held the appointments of junior casualty officer at the General Infirmary at Leeds and house-surgeon at Bradford Royal Infirmary. In April, 1939, he received a commission as a lieutenant in the R.A.M.C. Reserve of Officers and was mobilized on the outbreak of the second world war a few months later. Promotion to captain followed in 1940, and four years later he became a Regular. During his career in the R.A.M.C. he served in Madagascar and with Paiforce, the Middle East Land Forces, the Central Mediterranean Force, and with the Army Medical Directorate as deputy assistant director-general. In 1944 he was appointed M.B.E. for gallant and distinguished services in Italy, and in the following year he was mentioned in dispatches. When he met his tragic death he was on his way to attend a United States Army exercise as medical liaison officer of the British Joint Service Liaison (Army Staff) at Washington. West-Watson was an efficient, experienced, and popular officer, and his early death is a great loss to the R.A.M.C. A memorial service was held in the chapel of Queen Alexandra Military Hospital on July 27, 1954. He is survived by a widow and two children.

Dr. G. E. TILSLEY, who died on November 11, 1954, at Sheffield, where he had been in practice since 1934, was for some years before that a medical missionary in the Belgian Congo. He was 59 years of age. George Edwin Tilsley, whose parents were Plymouth Brethren, was born on July 10, 1895, the eldest of the seven children. He began the study of medicine at Bristol University with little material support but with the firm conviction that God would provide for his needs. After the first year he supported himself and paid his way by coaching fellow students, dispensing for general practitioners, and demonstrating anatomy. He played hockey for his university and was in the team that beat Oxford before the first world war cut short his sporting career. After qualifying M.R.C.S., L.R.C.P. in 1918 he remained as casualty officer at Bristol Royal Infirmary until called up, when he was sent to Salonika. He became staff officer in hygiene to the Army of the Black Sea and so remained until demobilization, when he returned to Bristol University for a short time as lecturer in pathology. His mind, however, was already turning to the mission field, and he went to Luanza on Lake Mweru in the Belgian Congo, where he built a hospital and also one of the first leper colonies in the Congo. His nearest colleagues were at the Government Hospital at Elizabethville, some 350 miles away. At first the people were somewhat suspicious of "the new medicine," but later on, as the news of successful treatment spread, they came in increasing numbers, and it was no unusual thing for patients to travel for six weeks in order to have a consultation. To feed the patients he established a farm and employed fishermen and hunters. In the early days Dr. Tilsley suffered much from malaria. During his second furlough he obtained the D.T.M.&H. in 1930, but in 1933 he retired from the mission field and in the following year acquired a small practice at Sheffield. He steadily enlarged the practice—his aim being ever to treat the whole man and not just the immediate disease. The advice his patients sought on matters other than medicine was willingly given. His interests were many, and he contributed much to problems concerning the well-being of the people generally, particularly in regard to road safety. Both his two sons are now doctors, and to them and to his widow and daughter the sympathy of his colleagues is extended.

The sudden death of Dr. D. C. DEVITT in a bathing accident at Hermanus, Natal, South Africa, on December 26, 1954, came as a shock to all who knew him. He was 48 years of age. Denys Christian de Wet (he changed his name to Devitt in 1933) was born at Cradock, Cape Province, the son of a well-known local medical practitioner, and came to England to enrol as a medical student at

St. Thomas's Hospital Medical School in 1927. After qualifying M.R.C.S., L.R.C.P. in 1932 he was in general practice at Eastcote, Middlesex, for some years, becoming also a medical officer to the Ruislip-Northwood Hospital, before deciding to specialize in anaesthesia. Later he became anaesthetist to Mount Vernon Hospital, an appointment he held for 10 years. He obtained the D.A. in 1942 and only last year he was elected a fellow of the Faculty of Anaesthetists. He served in the last war as a member of the R.A.F.V.R., attaining the rank of squadron leader, resigning his commission in 1948, the year after he returned to South Africa. In 1933 he married Christine Margaret, elder daughter of the late Dr. Charles Sampson.

We are indebted to Dr. J. C. NICHOLSON for the following appreciation: In South Africa, as senior full-time anaesthetist to the largest teaching hospital in the country—the Johannesburg Hospital—Denys Devitt played a prominent part in the development of modern anaesthesia. It was his work in that field which gained him the respect of all his colleagues; and his solid, practical approach to the most difficult problem was generally admired by all who were privileged to work with him. With his enthusiasm for progress he also displayed a shrewd conservatism, based on sound physiological principles, which was a sheet anchor to his pupils and enabled them, amid a maze of innovations, to sift the wheat from the chaff. His loss is irreplaceable, for he belonged to that rapidly disappearing group of men who are able to combine the breadth of vision and human understanding of a first-class general practitioner with the skill and judgment of the specialist. Those who were privileged to know him more intimately knew him as a kind and generous friend and as a devoted husband and father.

Dr. H. J. S. MORTON, who for the last few years had been living in retirement at Brinkley, near Newmarket, died in London on January 3 after a long illness. He was in his 70th year. Harold James Storrs Morton was born at Sheffield on January 31, 1886, the second son of the Rev. C. J. F. Morton, and was educated at Uppingham, Pembroke College, Cambridge, and the London Hospital. After gaining a second class in the Natural Sciences Tripos, he qualified by taking the conjoint diploma in 1912, graduated M.B., B.Chir. in 1916, and proceeded to his M.D. in 1919. After qualification he held a series of house appointments at the London Hospital until the outbreak of the first world war in 1914, when he took a commission in the R.A.M.C.(S.R.) and served in France till 1918. After a period as assistant medical officer at King Edward VII Sanatorium, Midhurst, he joined a practice at Bridlington, and remained there till 1935, when he moved to the St. John's Wood area of London. He retired from practice in 1947 and went to live in Brinkley, but continued to sit on medical boards till ill-health finally forced him to give up work altogether. Morton was an old international Rugby forward, having played for England in 1909 and 1910 and for Cambridge in 1908.

C. J. G. T. writes: I had the privilege of knowing Harold Morton intimately, as a fellow houseman at the London and later as a partner in practice for twelve years. Morton was a big man in every way, a typical Rugger forward in appearance, but in manner no one could have been more gentle. Quiet of voice, showing the utmost consideration for the feelings of others, self-effacing in company, the whole man rather belied his great and well-earned reputation on the football field, and this probably helped to give him the name "Tiny," by which he was known among his student friends. He possessed a droll sense of humour which delighted his associates. Morton was a very able and most conscientious doctor, who never spared himself when the interests of his patients demanded his services. He was a first-rate physician and a very capable anaesthetist. It is no exaggeration to say that he was universally beloved by his patients, and he had a perfectly wonderful way with old ladies, who simply adored him. He had no use whatever for the National Health Service Act, and gave up practice rather than have anything to do with it. He was a man of very high ideals, who was incapable of anything underhand, and he won the respect of all with whom he came in contact. Morton had to suffer grievous misfortune and disappointments, but never allowed these to sour him. He lost his first wife with tragic suddenness while she was bathing, and he was called to the beach not knowing that she was the victim. To a man of his temperament this was even a bigger blow than it would have been to many others, especially at a time when his three sons were at the difficult age when a mother can do so much for them. It was a comfort to his friends to know that his second marriage was such a happy one. We offer our profound sympathy to his widow and three sons.

The distress caused to his family and friends by the death on January 4 at St. Andrews of Dr. J. A. MACDONALD-SMITH was deepened 18 days later by the death of his widow, Dr. Elizabeth G. Macdonald-Smith, on January 22. Born on May 21, 1872, at Belfast, the son of John Smith, plumber, of Aberdeen, and Jane Smith, of Carrickfergus, John Alfred Smith was the eldest of a family of 13 and left school at the age of 14 to work in the Post Office, where he eventually became an expert telegraphist. His heart was set on becoming a medical missionary, and at first he attended night classes and later worked at night in the telegraph office so that he could attend lectures in the morning at Queen's University, where he began his medical education. In 1896 he went to Edinburgh to continue his training, helped by the Edinburgh Medical Missionary Society, and graduated M.B., Ch.B. in 1900. In the same year he went to India to establish a medical mission station at Rajshahi, Eastern Bengal, for the Presbyterian Church of England, and, overcoming many difficulties, financial and climatic he built a hospital and a mission bungalow at Naogaon. In 1901 he married Elizabeth Greer, the youngest daughter of the Rev. K. S. Macdonald, of Duff College, Calcutta. She had been a fellow student at Edinburgh University and graduated M.B., Ch.B. with distinction a year before him. During his first furlough, while doing deputation work for the Church's foreign missions, he found time to continue his postgraduate studies and took the F.R.C.S.Ed. in 1909 before returning to India. There was an interlude in his missionary service from 1914 to 1921, when he was in general practice at Nottingham. During part of this time he was also attached to one of the military hospitals in the district. When the educational future of his family was secure, Dr. Macdonald-Smith sailed for India again, this time to serve the Church of Scotland at Kalimpong, North Bengal, where he had to learn a new language and cope with new problems. He also found a new cause to fight for—the treatment and control of leprosy. In addition to his work at the Charteris Hospital he established, not without early opposition, a leper hospital and supervised its building on the hillside overlooking the Teesta valley with a magnificent view on all sides. Its reputation was quickly made, and patients came, sometimes long distances, from the surrounding states of Nepal, Bhutan, and Tibet. A church was also built at the tip of the spur and is a landmark for miles on either side, a lasting memorial to his perseverance and devoted service. On his retirement in 1939 he could not immediately return to this country on account of the war, so his offer of help in South India was gratefully received to enable other missionaries to take overdue holidays. He continued working, first in Chingleput and then in Sholinghur (for the Australian Presbyterian Church), until 1944, when, with his wife, he travelled home for the last time. Their retirement was spent in the home his father had made in Bangor, Co. Down, but towards the end they had been staying with their daughter at St. Andrews. Dr. Macdonald-Smith's long life was one of dedication to the overseas work of the Church in the field of medicine. Difficulties and disappointments were many, but he met and overcame them with courage, determination, and prayers. He was a man of high principles and inflexible purpose,

softened by a saving sense of humour. His wise counsels and his example will be sadly missed by many friends all over the world. His son, Dr. K. S. Macdonald-Smith, is in practice at Nottingham.

Dr. ELIZABETH G. MACDONALD-SMITH, who had been in failing health for a long time, did not long survive her husband, Dr. J. A. Macdonald-Smith, whose obituary is printed above, for she died on January 22 in her 79th year. Born at Calcutta on June 17, 1876, the youngest daughter of the Rev. and Mrs. K. S. Macdonald, Free Church of Scotland missionaries, Elizabeth Greer Macdonald had a distinguished career at Edinburgh University and graduated M.B., Ch.B. in 1899, soon after the degree in medicine had become available to women students. She preceded her fiancé to the mission field, and after their marriage in 1901 she was his constant helpmate in all his medical missionary work throughout their long life together. She will be remembered also in Nottingham, where, after her husband's return to India in 1921, she remained with her children for five years and was an assistant school medical officer in the city. Those who mourn the passing of Dr. and Mrs. Macdonald-Smith will remember with gratitude their useful life of service together, and will be glad that in their death they were not divided.

Dr. WILLIAM ARNOLD, who was in practice for many years at Waltham-on-the Wolds, near Melton Mowbray, died on January 3 in his 92nd year. William Arnold was born on May 13, 1863, and was educated at Trent College and Owens College, Manchester, qualifying in 1885 by taking both the M.R.C.S. and L.S.A. diplomas. He then held the appointment of junior house-surgeon at Ancoats Hospital, Manchester, before entering general practice at Blisworth, Northamptonshire, where he also performed the duties of medical officer to the Blisworth district of the Towcester Union. From Blisworth he moved first to Great Milton, in Oxfordshire, where he became medical officer to the Great and Little Milton districts of the Thame Union, and then to Crawley, in Sussex. About 1897 he settled in practice at Waltham-on-the-Wolds, becoming medical officer and public vaccinator for the district and medical officer to the Melton Mowbray Medical Club. In a very short time all who knew him in the hunting districts of Leicestershire came to revere and love him. He retired in 1933 at the age of 70, and, after a visit to his only son in Kenya, settled at Stratford-on-Avon to be near his married daughters. He found retirement very tedious, however, and in a few months' time was acting as locumtenent for friends, later buying another practice at Four Marks, in Hampshire, where he worked until the death of his wife in 1942. He then returned to Stratford-on-Avon to live with his youngest daughter.

Mr. ARNOLD LEEMING, who died at Bristol on January 9, was well known as a general surgeon both at Sudbury, Suffolk, and at Cheltenham. Born at Halifax, Yorkshire, in 1881, the son of an architect, Arnold Leeming was educated at the City of London School and at University College, London, before becoming a medical student at Guy's Hospital. There he was fellow dresser, under Mr. W. H. A. Jacobson, with the late Mr. E. C. Hughes, and he was house-surgeon to Mr. C. H. Golding-Bird just before the latter's retirement, Hughes being house-surgeon to Mr. (later Sir) Arbuthnot Lane at the same time. Leeming and Hughes remained warm friends for many years. After graduating M.B., B.S., with honours, in 1904, and holding a house-surgeoncy, he went to Sudbury as a locumtenent, but decided to stay there, and was for some years in partnership with Dr. H. D. King. He also became honorary medical officer to St. Leonard's Hospital, Sudbury, acquiring a high reputation for the emergency surgery he had to undertake. During the first world war he served in the R.A.M.C. as a surgical specialist at the 67th and 63rd General Hospitals in France and Salonika, attaining the rank of major. In 1922 he retired from private practice for a time, and then settled at Cheltenham with Mr. Thomas Holmes, another Guy's man, as a general-practitioner surgeon. Obtaining the F.R.C.S.Ed. in 1924, he was elected to the honorary surgical staff of Cheltenham General Hospital and for many years was medical officer to the Cheltenham Colleges. Particularly interested in the radium treatment of cancer, he did much good work as a surgeon, and his opinion was greatly valued by his colleagues and by practitioners in the surrounding district. He had a kindly nature and was extremely conscientious in his work. In his younger days he was a good cricketer and footballer: he played cricket for Guy's and later for the Suffolk County Club. He finally retired from practice in 1945 and went to live at Tankerton, in Kent, where he became keenly interested in gardening. He married Miss Anne Lamprey, and they had three daughters and one son, who is Dr. John A. L. Leeming, a dermatologist at Durban, Natal. His brother is Dr. A. Norman Leeming, and Dr. Donald N. Leeming and Dr. Roy A. Leeming are his nephews. All are Guy's men.

Dr. CECIL MEREDYTH JONES, a well-known Croydon general practitioner and for many years a surgeon at Croydon General Hospital, died on January 9 at the age of 64. From University College, Cardiff, he went on to the Westminster Hospital, and graduated M.B., B.S., with honours in medicine, in 1912. After working as house-surgeon at the Westminster Hospital and later at the Taunton General Hospital, he joined the R.A.M.C. at the outbreak of the first world war, being wounded in 1916. In 1921 he took the F.R.C.S., and in the following year settled in practice at Croydon in partnership with Dr. C. Poulett Harris and Dr. J. H. Thompson. Soon he was elected to the surgical staff of the Croydon General Hospital, where he continued his operative work until 1948. Although in failing health for the past two years, Dr. Jones was at work in his busy practice until about six weeks before his death. He leaves a widow and one daughter.

Dr. W. F. MUNRO, the senior medical practitioner in Burnley, died suddenly at his home there on January 18, aged 74. Born on March 20, 1880, William Fraser Munro was educated at Aberdeen University, graduating M.B., Ch.B. in 1903 and proceeding M.D. in 1929. Settling in Burnley in 1906, he was in active practice there until the day of his death, a span of almost 50 years. A member of the British Medical Association for 48 years, he was honorary secretary of the Burnley Division from 1921 to 1932 and chairman in 1932–3. He was a member of the Burnley Insurance Committee from 1929, and from 1947 a member of the Burnley Executive Council, being vice-chairman of the latter body since 1952. For 30 years he was a member of the local medical committee and had been chairman for the past 10 years. In spite of his busy professional life he found time for much public service. For 15 years he was a member of the town council, being chairman of many of its committees concerned with health matters. He was also a borough magistrate for many years. During the first world war he served with great distinction in the R.A.M.C., attaining the rank of lieutenant-colonel and being awarded the Military Cross in 1917. He received the Territorial Decoration in 1923. Keenly interested in the welfare of ex-Service men, he was president of the Burnley branch of the Old Contemptibles' Association for 25 years.

C. E. B. L. writes: At a crowded memorial service held in Burnley parish church Dr. Munro was described as "one of the most outstanding characters that Burnley had known this century." As one who has known him for many years as a colleague, I should like to add my humble tribute. Above all, William Fraser Munro was a man of good will; he loved his fellow men, understood their troubles, and in his own kindly way helped to lighten their burdens. In short he was, what so few of us manage to become, an outstanding example of the family doctor. As chairman of the medical committee he acted as a cushion, not to be sat

on, but to soften the verbal blows of conflicting views. Until his death he was most active both physically and mentally, and had no difficulty in fitting into the rapidly changing face of medicine. Through it all, his kindly smile, his courteous manner, and his quiet humour remained unaltered. He was most truly a gentle man. To his widow, son, and daughter we extend our deepest sympathy.

The death took place on January 30, at the age of 81, of Brevet-Colonel A. E. HAMERTON, who had spent 28 years of his life in the medical services of the Army, and afterwards served for 18 years as pathologist to the Zoological Society of London. Albert Ernest Hamerton took his medical training at the Leeds Medical School, qualifying in 1899. After a period as resident medical officer at Leeds Public Dispensary he joined the Army in 1900. In 1904, by which time he had attained the rank of captain, he saw active service in Somaliland, in the operations against the "Mad" Mullah, and he was in the battle at Jidballa when 1,000 of the enemy were killed and the British loss in killed and wounded was 58. For his services in that action he was mentioned in dispatches and received the D.S.O. From 1908 to 1910 he was a member of the Sleeping Sickness Commission in Uganda, and no sooner had he completed that task than he was sent on a similar commission to Nyasaland, which lasted until 1913. He joined the British Expeditionary Force in France at the outbreak of the first world war, and served until 1919; here again he was mentioned in dispatches and also received the C.M.G. From 1920 to 1922 he was director of the Central Laboratory and Pasteur Institute at Bagdad. Returning to this country in 1923, he became assistant director of pathology at the War Office. He retired from the Army in 1928 and took charge of the prosectorium at the London Zoological Gardens, where he performed innumerable post-mortem examinations on many species of animals. He had always taken an interest in comparative medicine and had written various papers on such subjects as rabies in Iraq and its treatment by carbolized vaccine, and on trypanosomiasis in man and beast in Africa. He was vice-president of the Section of Comparative Medicine at the Centenary Meeting of the British Medical Association in 1932. Colonel Hamerton served on the Council of the B.M.A. and on the Naval and Military Committee from 1929 to 1932, and did some very useful work on subcommittees concerned with conditions in the R.A.M.C. He was a Fellow of the Royal Society of Medicine, the Royal Society of Tropical Medicine and Hygiene, and the Zoological Society of London, and a member of the Pathological Society of Great Britain and Ireland.

Dr. J. H. MURDOCH, principal medical officer at Wandsworth Prison, died in St. James's Hospital, Balham, on January 22 at the age of 54. He had been in poor health for some years, but carried on with his work until a few days before his death. James Hunter Murdoch, a direct descendant of William Murdoch, the inventor of gas lighting, was born at Glasgow on May 27, 1900. He received his early education at Whitehill School and then volunteered, at the age of 17, for service in the Army during the first world war. On return to civilian life he entered Glasgow University as a medical student and graduated M.B., Ch.B. in 1924. In 1925 he was appointed resident medical officer at the Glasgow District Mental Hospital, where he was one of the first to become interested in the malaria therapy of general paralysis of the insane, later publishing his observations. He joined the prison medical service in 1928 and held appointments in various prisons throughout the country, gaining an increasingly high reputation as time went on. At Broadmoor he made a special study of crime in schizophrenia, publishing a paper on the subject in the *Journal of Mental Science* in 1933. In 1949 he and three other prison medical officers submitted a memorandum to the Royal Commission on Capital Punishment. Most of his work, however, must remain unknown to the general public, but while at Wandsworth he gave valuable expert advice in many well-known criminal cases. James Murdoch, before his illness, was a keen all-round games player. He was an enthusiastic amateur footballer and a good cricketer, golfer, and tennis player, and will be remembered by many senior prison officers for his stamina in these games. He spent many of his holidays camping and boating in Scotland. His ability extended beyond his own specialty, and he was ever ready to lend a helping hand to a local practitioner at short notice. He was an excellent companion and a sincere and reliable friend. His early death came as a great shock to all who knew him, and he is mourned not only by the prison staff but by a much wider circle of friends in Wandsworth. He is survived by a widow and daughter, who is a science graduate of St. Andrews University, and to them we offer our sincere sympathy.—T. J. L.

A memorial service for the late Dr. HAROLD K. WALLER will be held in the chapel of the British Hospital for Mothers and Babies, Samuel Street, Woolwich, S.E.18, on Thursday, February 17, at 3 p.m.

Medico-Legal

SURGEON PHYSICALLY FIT

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On February 3 the Court of Appeal Dismissed the appeal of Mrs. Winifred Nickolls against the Ministry of Health as successors under the National Health Service Act to the liabilities of the Royal Free Hospital. Mrs. Nickolls's case was that she was operated upon for the removal of a goitre on December 1, 1944, by the late Mr. Cecil Joll, who was then suffering from carcinoma of the lung, that he and the hospital authorities knew or ought to have known that his state of health was such that he was unfit to perform the operation, and that by reason of his unfitness the result of the operation was that she now suffered from permanent bilateral laryngeal paralysis because of damage to the recurrent laryngeal nerves.

Mr. Justice Gorman had dismissed the action on July 2, 1954, because he came to the conclusion that Mr. Joll had in fact been quite fit to perform the operation.

In his judgment dismissing the appeal Lord Justice Denning[1] said that Mr. Joll was at that time the greatest surgeon in England for that type of quite simple operation, during which in some way or other both Mrs. Nickolls's laryngeal nerves had been damaged, which was a very rare thing to have happened. Mrs. Nickolls said that the cause was Mr. Joll's state of health. In June, 1944, he was diagnosed as suffering from cancer of the lung. By September he was also suffering from diabetes and was having deep *x*-ray therapy and insulin. In November, 1944, the cancer was found to be spreading through his body, but he went on operating until January 9, 1945, and died 16 days later. He was a brave man who carried on with his work to the last possible moment. Mrs. Nickolls said that that would have been wholly admirable but for the fact that other people's lives were in his hands.

Lord Justice Denning felt that something must have gone wrong with the operation owing to Mr. Joll's illness, resulting in the damage to Mrs. Nickolls's laryngeal nerves, but that was not negligence unless it could be said that there was negligence every time a surgeon was taken ill in the theatre. There was no question of want of skill or care by Mr. Joll. The real question was whether he was fit to undertake the operation at all, for obviously surgeons should not undertake operations unless they were fit to carry them out. The judge had found that Mr. Joll was fit to perform this operation, and the Court of Appeal could not differ from him on that point.

Lord Justice Hodson delivered a concurring judgment, and Lord Justice Parker agreed.

[1] *The Times*, February 4, 1955.

OBSCENE PUBLICATIONS

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A committee appointed on the initiative of the Society of Authors to inquire into and report on the law relating to obscenity in literature has now submitted its principal recommendations to the Home Secretary in the form of a draft Bill. This is designed to remedy what the committee considers to be anomalies and defects in the existing law relating to the common-law misdemeanour of publishing obscene libels, the powers of justices to order the destruction of obscene matter under the Obscene Publications Act, 1857, and the powers of the Commissioners of Customs and Excise to destroy indecent matter seized on import.

The committee's objection to the present common law relating to obscenity is that the test to be applied in deciding whether the matter is obscene is purely objective: in the view of the jury is the matter calculated to deprave and corrupt those whose minds are open to its influence and into whose hands it may fall? The committee observes that the intention and purpose of author and publisher are ignored, that it is no defence that the matter is of literary, artistic, or scientific merit, that expert evidence of literary, artistic, or scientific value is not admitted, that it is not clear whether a work objectionable only in isolated passages rather than in its "dominant effect" can be obscene, that they think that horror, murder, violence, and sadism are not caught by the present law, and that maximum penalties are not defined.

While the force of the committee's objections from the point of view of authors, printers, publishers, and booksellers is plain enough, others may think that an objective test is perhaps not only right but the only one susceptible of practical application if there is to be any legal restriction on obscene publications at all.

The remedies proposed by the Bill are that the intention and general character of author and publisher are to affect the matter, and the court is required to consider the "dominant effect" of the publication, whether it has in fact corrupted anyone, its literary, artistic, or scientific merit, on which expert evidence is to be admissible, and the class of persons among whom it is likely to circulate. The word "obscene" is to cover matter which, whether or not concerned with sex, "unduly exploits" horror, cruelty, or violence. The maximum penalty for an offence is to be £100 or six months' imprisonment.

The chief objections to the procedure under the Obscene Publications Act, 1857, are in addition that author, publisher, and printer have no *locus standi* to defend their work; that neither the prosecutor in attacking the work nor the magistrates in condemning it are obliged to indicate what in it they consider to be obscene, and prosecutions can be instituted, as indeed they can for the common-law misdemeanour, without the blessing of the Director of Public Prosecutions. The committee's objections to the Customs and Excise powers are that they are exercisable by the commissioners without any judicial determination by magistrates and without reference to the Director of Public Prosecutions.

The proposed remedies are that magistrates, in making destruction orders, shall take into consideration the same matters which the court is to consider in trying a case of obscene libel, that the author, publisher, printer, and distributor shall all have the right to give and call evidence, that the Customs authorities shall act only on the issue of a destruction order by a magistrate, and that all prosecutions shall be subject to the consent of the Director of Public Prosecutions.

As to medical textbooks, even in the present state of the law, magistrates and jurors are not likely to confuse them with pornography.

SLIPPERY FLOOR

Because cleaners in a ward at St. John's Hospital, London, S.W., failed to warn Mrs. Rose Hannah Slade, aged 67, of the presence of polish on the floor, Mrs. Slade, who slipped on the polish and broke her right thigh, was awarded £781 damages with costs by Mr. Justice Finnemore in the Queen's Bench Division on February 3. His lordship held that the Battersea and Putney Group Hospital Management Committee were liable because of the negligence of their servants.

On October 27, 1953, Mrs. Slade was visiting her husband, who was seriously ill in the hospital and has since died. When she was leaving the ward she saw two women standing with mops but not working. She slipped on a patch of polish that had not been rubbed in and fell. Evidence was given that, according to the hospital's accident book, 16 persons had slipped or fallen on the polished floors of wards and corridors in 14 months.

In his judgment, Mr. Justice Finnemore said he was satisfied that Mrs. Slade slipped on a part of the floor where polish had been spread and not properly finished off. Someone should have warned her of the danger, but they did not. The patch of polish, of which Mrs. Slade was not aware, was a concealed danger, he said, especially in the absence of any warning. It was more slippery than after the floor had been polished. He was satisfied there was no negligence on Mrs. Slade's part in failing to notice the small difference in the appearance of the floor. She did not know there was an unusual danger there. Was it negligent to leave that polish on the floor without giving a person warning? He thought the hospital committee were negligent through their servants, who did not act with reasonable care or give the warning required.

Awarding £750 general damages, in addition to the £31 special damages agreed, his lordship said Mrs. Slade had permanent limitation of movement of her right hip, and was incapable of doing any work that involved kneeling or stooping.

CRITERIA OF LIABILITY

The First Division of the Scottish Court of Session on February 4 ordered a new trial in an action which arose out of the breaking of a hypodermic needle. In the course of his judgment the Lord President (Lord Clyde) made some observations[1] on the establishing of negligence, and remarked that the standard seemed to be the same in England as in Scotland. He said that, to establish liability by a doctor where deviation from normal practice was alleged, three facts required to be established. First of all it must be proved that there was a usual and normal practice. Secondly, it must be proved that the defender had not adopted that practice. Thirdly (and this was of crucial importance), it must be established that the course the doctor adopted was one which no professional man of ordinary skill would have taken if he had been acting with ordinary care.

Medical Notes in Parliament

CLEARING THE AIR

Clean air legislation has attained a place in the forefront of the political picture with the undertaking given on February 4 that a Government Bill, Beaver Report "in principle," would be introduced this session. So the campaign, which began with the outcry after the deaths and damage to health caused by the great fog in December, 1952, given formal shape by the investigations conducted by Sir Hugh Beaver and his committee, and political impetus from the Bill presented by Mr. Gerald Nabarro, the Conservative M.P. for Kidderminster, has achieved its first objective.

Mr. NABARRO, moving the second reading of his Clean Air Bill, traced the ineffective efforts made to deal with smoke pollution back as far as 1257, when Queen Eleanor was reported to have moved from Nottingham because of the fumes caused by the burning of sea coal. In bringing the record up to date with an examination of the economic

[1] *Scotsman*, February 5, 1955.

losses caused by smoke pollution—estimated by the Beaver Committee at £250m. a year—he went on to quote Mr. Edward MacLellan, a surgeon, who had advised him and made the following statement: "It has been established beyond reasonable doubt that the alarming increase in the incidence of cancer of the lung is associated with the fouling of the atmosphere by smoke, exhaust fumes, and the offensive and deadly eructations of gas works, power stations, and so on. There are more than twice as many victims of cancer of the lung in the towns as in the country, and the mortality from lung cancer among workers in the gas industry is double that of the general population."

Mr. Nabarro quoted also the Beaver Report on the medical aspects of smoke pollution. He declared that he and his supporters wanted an assurance from the Government that they would introduce a comprehensive and effective measure during the present session of Parliament.

Mr. ALFRED ROBENS (Blyth, Lab.) gave the Opposition's blessing in advance to such legislation.

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) moved the rejection of Mr. Nabarro's Bill, but only because, as a private Member's Bill, it could not go far enough and lacked the essential financial provisions. Even to assume that in ten years an 80% reduction of atmospheric pollution could be achieved meant that there was no time for delay and that no half-measures could be tolerated. Most authorities would agree that the worst pollution was sulphur dioxide, either by its own action as an isolated gas or through its synergic effects when it combined with sulphuric acid mist. He wondered whether the substitution of oil for coke in central heating plants would not inevitably mean a greater concentration of sulphur dioxide in the hearts of cities, since the 4% sulphur in oil compared with the 1½% in coke would mean more sulphur fumes in the air, unless costly preventive action was taken.

Mr. SOMERVILLE HASTINGS (Barking, Lab.) expressed his belief that the results of polluted air on health were almost entirely due to sulphur oxides and his doubt whether these would be appreciably decreased by the Bill.

Mr. DUNCAN SANDYS, Minister of Housing and Local Government, stated the Government's views, and gave the promise of their own Bill. Consultations with industry and local authorities were going ahead satisfactorily, but were not yet complete. Mr. Nabarro's text differed in many ways from the Beaver proposals, would present many difficulties, and could not of necessity contain the financial teeth to make it effective. But there was general agreement on the policy, and when its consultations were concluded the Government would frame and introduce a comprehensive measure on the general lines of the Beaver Report, which he hoped would be completed this session.

Mr. NABARRO exclaimed, "That is all we wanted," Dr. STROSS withdrew his motion for rejection, and Mr. NABARRO withdrew his Bill.

Colouring Matter in Food

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Food on January 31 what type of dye was used for the purpose of colouring some types of sugar purple, yellow, and green; and whether he would make a statement on the possible dangers to health that are involved. Dr. CHARLES HILL, Parliamentary Secretary, Ministry of Food, said that the Public Health (Preservatives in Food) Regulations forbade the use of five named coal-tar colours, but he had no reason to suppose that any one of these was being used in the coloured sugars in question. If Dr. Stross had any information to the contrary he would be glad to have it.

Mr. JOHN RANKIN (Glasgow, Tradeston, Lab.) asked the Minister of Food what steps he was taking to control the colouring materials put into foodstuffs so as to ensure that no substances deleterious to human health would be added. Dr. CHARLES HILL replied that the use of certain colouring matters including certain coal-tar colours was already prohibited. A report of the Food Standards Committee on the addition to foods of colouring matters, including coal-tar colours, had recently been published. As was customary, it was proposed to await representations from interested parties before reaching a decision on the committee's recommendations.

Fluoridation Tests

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister of Health whether the Anglesey water authority had yet investigated for fluorine content the urine of the area in which fluoridation was to be introduced, and the urine of the control area; how many persons participated in this investigation, and what were their ages; how far the condition of teeth of infants and older children in the areas had been ascertained; and if he would ensure that accurate and consecutive records of fluorine content of urine, and condition of teeth, were kept in the two areas. Mr. IAIN MACLEOD stated on February 3 that a pilot study of urinary excretion of fluoride in children in this country confirmed the result of work done in the United States and New Zealand, and made it clear that more exclusive studies need not be undertaken before fluoridation in Anglesey was begun. Arrangements were being made to examine the teeth of samples of children in each age group up to and including 15 years (and to some extent of adults), and consecutive records would be kept of all the most relevant facts.

Hospital Administration Report

Mr. J. K. VAUGHAN-MORGAN (Reigate, Con.) asked the Minister of Health whether he had considered the report of the committee of the Central Health Services Council on the internal administration of hospitals.[1] Miss PAT HORNSBY-SMITH, Parliamentary Secretary, stated on January 31 that the Minister had studied the report with great interest. It contained much useful material and many valuable suggestions, most of which were addressed primarily to the hospital authorities themselves and were for them to consider in the light of their own particular circumstances.

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked if the Minister was prepared to make a statement on the observations of the Central Health Services Council with regard to medical superintendents of mental hospitals. Miss PAT HORNSBY-SMITH replied that the Minister did not consider it would be appropriate at the present time to introduce model standing orders for the general government of mental, and mental deficiency, hospitals defining the functions of the medical superintendent.

Paying and Non-paying Patients

The MINISTER OF HEALTH informed Mr. SOMERVILLE HASTINGS (Barking, Lab.) on February 3 that at the end of 1953 the number of beds in England and Wales designated under section 5 of the Health Service Act was 1,550 in teaching hospitals and 3,697 in other non-mental hospitals. The average daily occupancy during 1953 was—teaching hospitals: paying patients, 967.5, non-paying patients, 217; other (non-mental) hospitals: paying 1,630, non-paying 720. Figures for 1954 were not yet available.

Scottish Surgeries

Mr. W. HAMILTON (Fife, West, Lab.) asked the Secretary of State for Scotland on February 1 what progress had been made in the talks designed to effect improvements in conditions at doctors' surgeries. Commander T. D. GALBRAITH, Under Secretary, said that it had been arranged that executive councils in Scotland would undertake a review of consulting accommodation in all areas where adequate arrangements for this purpose had not already been instituted.

Mr. HAMILTON asked for an indication of when some positive action would be taken. There were complaints about unsatisfactory conditions in surgeries, and some firm action

[1] *British Medical Journal Supplement*, October 2, 1954, p. 133.

was necessary. Commander GALBRAITH said he could not give any assurance. He knew what the situation was, and he hoped the executive councils would get on as quickly as possible.

Cadmium Poisoning.—The question whether, in the light of the report by a member of the staff of the Medical Research Council, cadmium poisoning should be prescribed as an industrial disease, and if so, for what occupations, is being referred to the Industrial Injuries Advisory Council.

Universities and Colleges

UNIVERSITY OF OXFORD

The title of Clinical Lecturer in the Diseases of the Ear, Nose, and Throat conferred upon Dr. R. G. Macbeth for five years from the first day of Michaelmas Term, 1954, has been changed to Clinical Lecturer in Otolaryngology.

The following degrees were conferred in Congregation on December 11:

D.M.—C. P. Silver.

B.M.—J. Billingham, A. C. Markus, B. Clarke, R. R. Charlwood, G. Harris, B. L. D. Phillips, E. J. Bovett, D. J. Reid, J. H. Baron, M. P. Joyston-Bechal, P. H. Merry, D. C. Beckingham, F. W. Wright, G. Appleyard, R. B. Chalmers, G. H. Fairley, J. Gerrard, D. Guttmann, L. I. Holmes-Smith, W. H. Mitchell-Banks, A. D. Jose, V. Marks, J. C. M. Wilkinson, E. J. Wimperis, C. M. S. Coppin, J. A. Mitchell, H. R. Overy, H. R. Dingle, M. Hartog, P. T. Pickens, H. J. Liebeschuetz, R. N. P. Sutton, P. J. Mitchell, D. T. Cousins, P. R. Samsworth, D. P. Woods, R. Akroyd, T. J. D Cochrane, Mrs. Elspeth A. Beckett, Mrs. Jean O. Hunter, Ann C. M. Wickham, Patricia J. M. Cotter, *D. H. Crill, *H. L. Freeman.

* In absence.

UNIVERSITY OF CAMBRIDGE

In Congregation on December 11, 1954, the degree of M.D. was conferred on J. J. Fleminger.

On December 20, 1954, the degree of B.Chir. was conferred on:

J. N. Godlee, P. J. Burrows, M. S. Robson, P. J. D. Kirk, C. E. Salter, E. F. D. Gawne, D. W. Atkinson, I. H. Backhouse, I. McL. Flowers, A. C. Johansson, I. V. Longfield, D. B. R. Osbourne, R. J. C. Pearson, D. J. H. Prosser, W. Atherton, L. H. Blonstein, P. D. Crockatt, R. H. S. Gibbs, A. M. Parfitt, M. J. Turner, J. F. Walker, R. D. Hyde, I. Ross Russell, W. L. Cordeaux, G. C. Spackman, A. H. Labrum, J. N. Bodger, P. G. T. Bye, W. S. Ogden, J. W. Blaxill, W. R. P. Bourne, J. A. Dryden, J. Fairley, L. H. Hurrell, C. F. Ridley, R. C. Nainby-Luxmoore, T. R. Clendon, J. S. Garfield, E. Redfearn, I. R. Robertson, G. F. W. Swan, S. T. G. Butterworth, D. H. Cameron, J. R. Burwell, J. S. Miller, R. Schram, Inez R. Aldous, Claudia M. B. Grigson.

On December 22, 1954, the degree of M.B. was conferred on:

G. H. Hilton, J. K. Snell, J. Crook, C. M. McGregor, G. F. B. Birdwood, D. J. Buttery, R. H. Gibbon, R. J. Knight, R. C. Lawson, W. A. Williamson, S. P. Lock, H. C. Masheter, J. T. Gibbs, P. D. W. Wickenden, S. G. Bayliss, J. W. Harding, H. Jacobs, I. G. Tait, W. H. Carling, D. E. Tunnadine, J. R. Wood, Mrs. Lucy M. Rochelle.

UNIVERSITY OF LONDON

The following candidates at the Institute of Psychiatry have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—Valerie A. Cowie, I. J. MacDonald, *M. I. M. Pines. The following have passed in Part I only: G. P. S. Fernando, F. Grunberg, R. R. Mowat, I. C. L. Patch, B. P. Shah.

The degree of M.D. was awarded on December 15, 1954, to P. J. Hare.

The John Marshall Fellowship in Surgical Pathology, tenable for two years in the first instance at University College Hospital Medical School, has been awarded from October 1, 1954, to Mr. D. B. Griffiths, F.R.C.S., who will also hold the Whait Fellowship awarded by the Medical School.

The following candidates have been approved at the examinations indicated:

M.D.—*Part I:* H. Barkley, P. J. A. Butcher, J. A. Cheese, H. W. D. Davies, S. Dische, Yvette A. P. Franklin, Eva A. Frommer, A. A. Glynn, N. D. Gower, L. H. Harris, J. M. Hinton, N. B. Kreitman, S. Mattingly, A. R. May, Ariela Pomerance, M. E. A. Powell, A. Trueman, H. J. Wyatt, Joan F. Zilva.

M.S.—*Part I:* N. C. Rogers.

*Awarded a mark of distinction.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examinations indicated:

M.D.—A. G. W. Branch.

FINAL M.B., CH.B.—H. T. Apsimon, P. H. Barry, Catherine A. Clark, D. J. C. Felton, J. H. L. Griffin, M. L. Harvey, J. K. Howell, Antoinette R. Joseph, J. McC. Laltoo, Jean D. Matthews, T. N. Matthews, J. H. Orr, B. K. Palmer, B. A. Poley. *In Group I completing the examination:* Pamela M. Atkinson, K. G. Collins, E. C. Skeens. *In Group II only:* R. G. McCormick.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **January 22** (No. 3) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	8	0	6	0	1	18	0	9	0	
Dysentery	482	65	227	22	4	490	100	178	18	2
Encephalitis, acute	4	0	1	0		4	1	1	0	
Enteric fever: Typhoid	1	1	0	0	0	3	0	0	1	
Paratyphoid	2	0	1	0	1	4	0	0	0	
Food-poisoning	119	10		0		148	17		0	
Infective enteritis or diarrhoea under 2 years				12	19				17	19
Measles*	7,038	656	557	557	52	1,106	12	43	31	132
Meningococcal infection	32	1	9	1	1	43	5	12	2	3
Ophthalmia neonatorum	28	0	6	0		28	0	2	0	
Pneumonia†	929	67	294	7		809	44	323	3	5
Poliomyelitis, acute: Paralytic	16	2	3	0	1	30	1	6	0	5
Non-paralytic	8	0				7	1			
Puerperal fever§	240	47	12	0		257	24	12	1	2
Scarlet fever	650	37	105	49	24	1,138	51	181	44	29
Tuberculosis: Respiratory	625	70	156	22		741	72	145	19	
Non-respiratory	75	5	21	2		92	6	20	3	
Whooping-cough	2,002	143	215	27	31	2.357	85	404	49	68

DEATHS in Great Towns	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	1	0		0		0	0		0	
Encephalitis, acute	0	0			0		0			0
Enteric fever	12	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	12	2	1	0	1	6	1	1	0	0
Influenza	136	13	4	1	0	31	4	5	1	2
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		2	0				2	0		
Pneumonia	557	88	37	15	7	356	52	37	14	13
Poliomyelitis, acute	1	0			1	5	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	129	15	14	4	5	123	17	13	1	5
Non-respiratory		3	1	0	0		0	3	0	2
Whooping-cough	3	1	1	0	0	2	0	1	0	0
Deaths 0–1 year	230	29	37	9	15	279	34	41	17	12
Deaths (excluding stillbirths)	8,185	1201	876	181	206	6,568	970	734	133	189
LIVE BIRTHS	7,535	1126	921	195	386	7,632	1148	918	214	370
STILLBIRTHS	218	20	26			206	21	17		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Typhoid in Yorkshire

In December, 1954, and January this year an outbreak of typhoid occurred in Pickering, Yorkshire. Probably 29 people have been infected; of these, 23 are primary cases and the other 6 family or household contacts; 28 are adults. We are indebted for the following information to Dr. W. R. M. COUPER, M.O.H. of Pickering:

The date of the onset of the primary cases was between December 17 and 24. On December 13 an epidemic of what seemed to be an upper respiratory infection began in Pickering and was labelled influenza. Later the infection spread to the surrounding districts. At first children were affected; then older people had the infection in a rather more severe form. Pulmonary complications were treated with chloramphenicol. In due course some of the cases were diagnosed as typhoid fever. The clinical picture was of pyrexia, nose-bleeds, headaches, and prostration. Five patients who presented this clinical picture were sent into hospital between December 31, 1954, and January 16 last. By February 1 *Salmonella typhi* had been isolated from the faeces of one patient, and investigation of this patient and of four others showed that infection was recent.

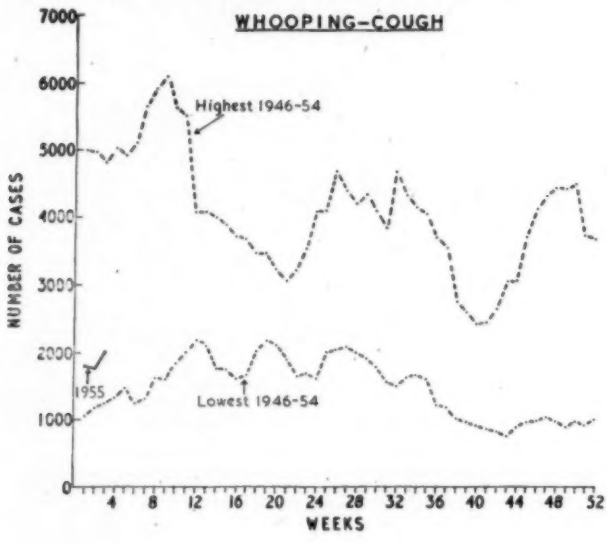
The epidemiological picture was of a localized outbreak from a single source of infection within a short period. Examination of affected and suspected persons excluded the water supply and milk as cause of the outbreak. A common food was eaten by all patients identified as primary cases, and investigations are continuing to find out how the material became contaminated.

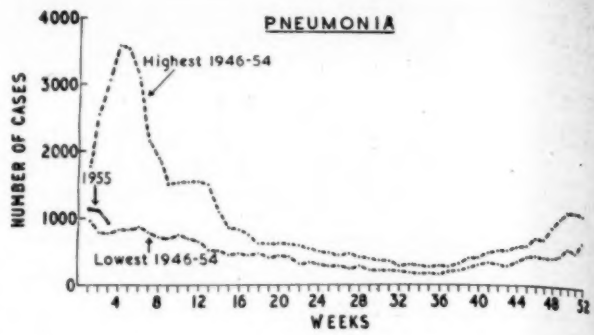
Influenza

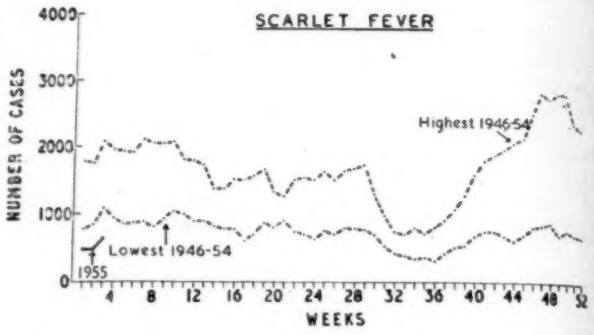
In the great towns of England and Wales the number of influenza deaths (123) in the week ending January 29 showed a decrease of 13 compared with the previous week. There were small increases in London and the south-east and in the north, east, and west Ridings, north midland and south-western regions, and in Wales, which were more than offset by decreases elsewhere, mainly in the north-western and midland regions. There is little change in the situation.

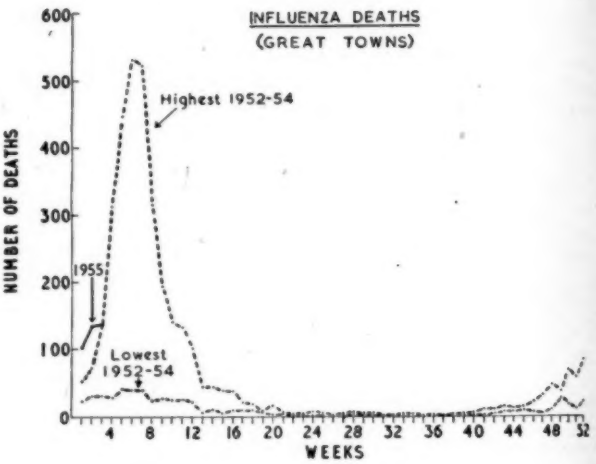
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine years 1946–54 (influenza, 1952–4) are shown thus - - - - - -, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending January 22 were decreases of 762 for measles, from 7,800 to 7,038, and 192 for acute pneumonia, from 1,121 to 929, and increases of 233 for whooping-cough, from 1,769 to 2,002, 185 for scarlet fever, from 465 to 650, and 80 for dysentery, from 402 to 482.

The largest falls in the number of notifications of measles were 135 in London, from 791 to 656, 122 in Lancashire, from 2,032 to 1,910, 110 in Essex, from 463 to 353, 99 in Cheshire, from 466 to 367, and 88 in Derbyshire, from 302 to 214. The largest increases in the incidence of whooping-cough were 33 in Kent, from 108 to 141, and 31 in Yorkshire West Riding, from 51 to 82. A small rise in the incidence of scarlet fever occurred throughout the country, the largest was 22 in Essex, from 27 to 49. 8 cases of diphtheria were notified, being 6 fewer than in the preceding week.

24 cases of acute poliomyelitis were notified, and these were 1 more for both paralytic and non-paralytic cases than in the preceding week. The largest returns were 3 in each of the counties of Essex, Lancashire, and Gloucestershire (Bristol C.B. 2).

The largest centres of dysentery were Lancashire 103 (Liverpool C.B. 22, Manchester C.B. 18, Oldham C.B. 12), Yorkshire West Riding 80 (Leeds C.B. 55, Sheffield C.B. 13), London 65 (Southwark 18, Chelsea 11), Middlesex 28,

Glamorganshire 26 (Cardiff C.B. 14, Swansea C.B. 9), Norfolk 26 (Norwich C.B. 17), Northumberland 23 (Newcastle-upon-Tyne C.B. 9), and Durham 20.

The deaths from influenza in the 160 great towns numbered 136, being 2 more than in the preceding week. The largest return was 13 in Birmingham C.B.

Week Ending January 29

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 745, whooping-cough 2,237, diphtheria 23, measles 10,697, acute pneumonia 1,062, acute poliomyelitis 23, dysentery 678, paratyphoid fever 4, and typhoid fever 9.

Venereal Diseases

In England and Wales during the quarter ending September 30, 1954, 1,281 new cases of syphilis were reported as attending the clinics. Of these, 190 were classified as primary, secondary, or latent in the first year of infection. 9 cases of congenital syphilis in children aged under 1 year were reported, and 158 cases in persons over that age. New cases of gonorrhoea numbered 4,821, of chancroid 79, and of non-gonococcal urethritis (males only), 3,644.—*Monthly Bulletin of the Ministry of Health*, January, 1955.

Smallpox in France

The total number of cases so far reported in the Morbihan Department is 66, including 14 deaths. In addition, one case is reported from Rennes in the Ille-et-Vilaine Department, which adjoins Morbihan, and two cases in the town of Saint-Die, Vosges Department.

Death Rate Variations

Geographical differences in death rates are noticeable for many diseases in England and Wales. They are among the analyses of vital statistics included in the text volume[1] of the *Statistical Review* for 1951 published this week, in which the pre-war practice is resumed of combining civil with medical statistics. In the age group 0 to 4 Greater London had the lowest general death rate and Wales the highest, while the north of England was in between. These disparities remain much the same for all age groups, though in some the south of England had slightly better statistics than Greater London. The differences by region are on the whole greater than the differences by density of population, and they are greater for males than for females. The lower death rates in Greater London and the midlands than elsewhere are thought possibly to be due to the benefits of suburban living.

Diseases of the respiratory system are well known to cause proportionately many more deaths in the north than in the south; so also do heart diseases, in particular coronary arteriosclerosis—Wales again showed a high incidence of this group of diseases.

Notifications of respiratory tuberculosis are more numerous in Wales, the north of England, and London and the south-east than in other parts of the country. The excess in Wales and the north is probably genuine; that in England and the south-east is thought to be a reflection of better diagnostic facilities. Mortality is exceptionally high on Merseyside, Tyneside, and in several midland cities. In 1951 the rate per million population was 512 in Liverpool, 463 in Sunderland, and 541 in Walsall, yet in London and the south-east it was 185, in Bath 177, and in Huddersfield 132.

A comparison of death rates from cancer of the lung with those from all forms of cancer shows that Greater London and the Merseyside cities have a higher proportion of deaths from lung cancer than other parts of England and Wales. Of the rural areas (where lung cancer is less prevalent than in cities), the south of England has the highest proportion of lung cancer deaths.

[1] *Registrar-General's Statistical Review of England and Wales for the Year 1951*, Text Volume (H.M.S.O., 10s.).

Medical News

Dr. E. D. Adrian, O.M., P.R.S., who was awarded a barony in the New Year Honours, becomes Baron Adrian, of Cambridge in the County of Cambridge.

New Midwives Rules.—Compulsory courses of instruction are ordered by the new midwives rules, issued as S.I. No. 120, 1955 (H.M.S.O. 1s. 3d.). Attendance at the courses is required of all practising midwives from 1958 every five years; midwives enrolled before 1938 must attend a refresher course within 12 months of giving notice to practise, unless they have attended one within five years. The rules also permit midwives to administer trichlorethylene.

New Journal.—The *Central African Journal of Medicine* makes its appearance as representative of medicine in the new Federation of Rhodesia and Nyasaland. It is a well-produced publication; its first number includes forewords by the Prime Minister of the newly formed Rhodesia and Nyasaland Federation (Sir GODFREY HUGGINS, F.R.C.S.), Sir RUSSELL BRAIN, P.R.C.P., and Dr. MORRIS, Federal Secretary of Health. Appropriately, a biographical note on David Livingstone appears, the first known medical man to practise in what is now Rhodesia and Nyasaland, and there are also papers on clinical subjects. Edited by Dr. M. GELFAND, the journal will appear six times a year at an annual subscription of £2 2s. Its editorial address is P.O. Box 2073, Salisbury, S. Rhodesia.

Dermatology Medal.—The Chesterfield Medal, with a cash prize of £25, is offered by the Institute of Dermatology for the best essay on a dermatological subject selected by the candidate. Full details from the Institute, at St. John's Hospital for Diseases of the Skin, Lisle Street, Leicester Square, London, W.C.2.

Essay on Health Visitors.—The Royal Sanitary Institute offers a prize of fifty guineas for an essay on "How the Health Visitor can help the family towards its full development." Full details from the Institute at 90, Buckingham Palace Road, London, S.W.1.

Scholarships Abroad.—Over 100 scholarships are offered to British students by 17 foreign countries for study abroad during the academic year 1955–6. The awards generally provide for free tuition and maintenance, and are tenable for periods varying from a few weeks to 12 months. The countries offering them are Austria, Belgium, Brazil, Denmark, Finland, France, Germany, Iceland, Italy, the Netherlands, Norway, Persia, Portugal, Spain, Sweden, Switzerland, and Yugoslavia. Closing dates for applications differ for each country, the earliest being March 7. Further information and application forms, for which a stamped, addressed foolscap envelope should be sent, may be obtained from the Education Division, British Council, 65, Davies Street, London, W.1.

Induced Hypotension.—The Edinburgh Postgraduate Board for Medicine will hold a fortnight's course of lectures and demonstrations on induced hypotension in anaesthesia at the Department of Anaesthesia, Royal Infirmary, Edinburgh, from March 21 to April 1 (see advertisement page 46). Applications to be sent before March 1.

D.D.T. Awards.—The Royal Commission on Awards has recommended an award of £6,000 for the manufacture of D.D.T., to be made jointly to J. R. Geigy, S.A., of Basle, and the Geigy Co. Ltd., of Manchester.

Dr. T. R. R. Mann, F.R.S., has been appointed director of the Unit of Reproductive Physiology and Biochemistry at Cambridge.

Dr. J. N. Hunt, senior lecturer at Guy's Hospital Medical School, has been appointed to the university readership in physiology tenable at that school.

Dr. P. M. Daniel has been appointed honorary consultant in neuropathology to the Army at home.

COMING EVENTS

Symposium on Cardiovascular Surgery.—There will be 60 participants from 17 countries at the International Symposium in Cardiovascular Surgery to be held in Detroit from March 17 to 19. The following subjects will be discussed: Diagnosis and Treatment of Pulmonary Stenosis; International Septal Defects; Late Results of Mitral Commissurotomy; Hypothermia; and Substitutes for Arterial Segments. Sir RUSSELL BROCK will be the speaker at the dinner meeting on March 18.

International Congress on Embryology.—The editorial board of the *Journal of Embryology and Experimental Morphology* has arranged an international congress in Brussels from April 4 to 7. Details from Dr. D. R. NEWTH, Department of Zoology, University College, London.

Laboratory Animals Bureau Symposium.—The third symposium will be held at the Royal Society of Medicine, London, W.1, on May 9. The subject will be "The Breeding of Laboratory Animals." The symposium is primarily intended for medical, veterinary, and scientific graduates.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, February 11

SOCIETY OF MEDICAL OFFICERS OF HEALTH: WELSH BRANCH.—At B.M.A. House, 195, Newport Road, Cardiff, 6.30 p.m., Dr. G. Grant: Student Welfare in the U.S.A.

Monday, February 14

CHADWICK TRUST.—At Royal Institution, 5.30 p.m., Sir Hugh Beaver: Clean Air.

LONDON UNIVERSITY.—At Senate House, 5.30 p.m., special university lecture in psychology by Professor Otto Klineberg (Columbia University): Psychology and International Relations.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Dr. W. G. Oakley and Mr. S. M. Cohen: Diabetic Gangrene.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—7.30 p.m., Dr. K. R. Capper, Ph.D., B.Pharm.: British Pharmaceutical Codex, 1954, and the National Formulary, 1955.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Hunterian Oration by Sir Cecil Wakeley: Hunter and Surgical Research.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 4.45 p.m., Dr. E. E. Snell (Texas): Relationship of Structure to Catalytic Activities of Vitamin B_6.

Tuesday, February 15

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor J. N. Davidson: Nucleoproteins in Cell Structure.

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 8.30 p.m.. Debate: That in the opinion of this House, the National Health Service is not in the best interest of the patient or the doctor. For the motion: Dr. J. L. McCallum; seconded by Dr. R. M. Noordin. Against the motion: Dr. Bruce Cardew; seconded by Dr. Arnold Elliott.

INSTITUTE OF DENTAL SURGERY.—At Eastman Dental Hospital, 5.30 p.m., Dr. H. M. Seldin, D.D.S. (New York): Oral Lesions of Interest to Dentist and Physician.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. J. Wallace: Bullous Eruptions.

LONDON UNIVERSITY.—(1) At University College Hospital Medical School, 5 p.m., special university lecture in medicine by Professor Jan Waldenström (Lund): Clinical Investigations in Hypergammaglobinaemia. (2) At Senate House, 5.30 p.m., special university lecture in psychology by Professor Otto Klineberg (Columbia University): Uses and Limitations of the Experimental Method in Social Psychology.

OXFORD UNIVERSITY MEDICAL SOCIETY.—At Radcliffe Infirmary, 8.15 p.m., general meeting.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Professor D. M. Pryce: Gynaecological Pathology.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Professor Alan Moncrieff: Marasmus.

Wednesday, February 16

EUGENICS SOCIETY.—At Royal Society, Burlington House, W., 5.30 p.m., Mrs. Judith Hubback, M.A.: Fertility of Educated Women.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Clefts, Vesicles, and Bullae.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. A. C. Morson: Non-Tuberculous Infections of the Renal Tract.

LONDON UNIVERSITY.—At Warburg Institute, 5.30 p.m., Dr. D. P. Walker: The "Astral Body" in Renaissance Medicine.

MIDLAND MEDICAL SOCIETY.—At Queen Elizabeth Hospital, Birmingham, 8.15 p.m., clinical meeting.

NORTH-WESTERN TUBERCULOSIS SOCIETY.—At Aintree Hospital, Liverpool, 5.30 p.m., Mr. J. Cosbie Ross: Renal Tuberculosis.

ROYAL MICROSCOPICAL SOCIETY.—5.30 p.m., Dr. E. S. Horning: Hormones in Relation to Cancer. Demonstration by Mr. G. N. Byford and Mr. A. C. G. Best: New Type of Mercury-vapour Lamp.

ST. MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE.—5.30 p.m., Dr. R. D. Newton: Indications for Psychological Treatment in Early Childhood.

Thursday, February 17

BASINGSTOKE PLASTIC CENTRE MEDICAL SOCIETY.—At Rooksdown House (Park Prewett Hospital), Basingstoke, 7.30 p.m., symposium: Fractures of the Long Bones with Soft-tissue Loss. Speakers, Professor J. Trueta, Mr. J. S. Ellis, Mr. A. J. Evans, and Mr. E. W. Peet.

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Dr. A. Robinson Thomas: Technique of Sialography; Mr. R. T. Payne: Experiences of Sialography.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor J. H. Gaddum, F.R.S.: Effects of Alcohol.

EDINBURGH CLINICAL CLUB.—At 7, Drumsheugh Gardens, 8 p.m., Mr. John Bruce: Surgery of the Stomach and Duodenum.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Techniques in Diagnosis of Fungous Infections.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., demonstration of specimens and cases.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. W. H. Bradley: Man and Virus.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At 26, Portland Place, London, W., 7.30 p.m., Colonel H. W. Mulligan: Recent Investigations on Trypanosomiasis in British West Africa.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Medical School, Small's Wynd, Dundee, 5 p.m., Mr. A. Logan: Benign Ulceration of the Oesophagus.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. M. A. Partridge: psychiatry demonstration.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 4.45 p.m., Dr. S. R. Elsden: Respiratory Mechanisms in Bacteria.

Friday, February 18

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 5 p.m., Dr. David Sutton: Thoracic Aortography by Percutaneous Transcarotid Catheterization; Dr. Conway J. Don: Intravenous Cholangiography After Cholecystectomy.

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. D. I. Williams.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. Smart: Pulmonary Tuberculosis.

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. G. J. Romanes: Motor Cells of the Spinal Cord.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., meeting in honour of Leonard P. Mark (1855-1930), author of "Acromegaly: A Personal Experience." Speakers Dr. A. W. Spence and Sir James Paterson Ross.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 2 p.m., Mr. D. M. Wallace: Natural History of Bladder Tumours. (2) 4 p.m., Professor C. H. Stuart-Harris: Virus Diseases of the Respiratory Tract.

● ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Mr. Iain McLennan: Some Surgical Aspects of Thyroid Disease.

ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Professor J. Chassar Moir: Confinements of Some English Queens and their Effect on History.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, 5.30 p.m., Professor F. Bergel: Attempts at Chemotherapy of Malignant Diseases.

Saturday, February 19

BIOCHEMICAL SOCIETY.—At London School of Hygiene and Tropical Medicine, 11 a.m., symposium: Biochemistry of Vitamin B_{12}.

APPOINTMENTS

MANCHESTER REGIONAL HOSPITAL BOARD.—F. Robinson, M.B., Ch.B., F.R.C.S., additional maximum part-time Consultant Plastic Surgeon to South Manchester Hospitals; G. Freeman, B.M., B.Ch., F.R.C.S., D.L.O., Part-time Consultant Ear, Nose, and Throat Surgeon to Lancaster and Kendal Hospitals; R. C. Woodcock, M.B., Ch.B., D.C.P., D.Path., Additional Consultant Pathologist, Bolton and District Hospitals; A. Kilpatrick, L.R.C.P.&S Ed., D.A., D.Obst.R.C.O.G., Assistant Anaesthetist, Lancaster and Kendall Hospitals; G. J. H. L. Hall, M.B., Ch.B., D.P.H., D.C.H., Assistant Physician (Infectious Diseases), Ladywell Hospital, Salford, and Astley Hospital, Wigan; G. H. Waddington, M.R.C.S., L.R.C.P., D.M.R.D., Assistant Radiologist, Lancaster and Kendal Hospitals; H. Ferguson, M.B., Ch.B., D.M.R.D., Assistant Radiologist, Blackburn and District Hospitals; G. H. A. Simmons, F.R.C.S., Consultant Surgeon to Crumpsall Hospital, Manchester; C. C. D. Martin, M.Ch., F.R.C.S.I., Senior Casualty Officer, Bury and Rossendale Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Halnan.—On January 30, 1955, at University College Hospital, London, W.C., to Margaret (formerly Booth), wife of Dr. Keith Halnan, a daughter—Susan Mary.

Ringrose.—On January 23, 1955, at St. Brenda's Nursing Home, Bristol, to Dora (formerly Lemmon), M.B., B.Chir., wife of David F. Ringrose, L.D.S., of Bitton, Glos, a daughter.

Turner.—On January 31, 1955, at Burnley, Lancs, to Dr. Helen Turner, wife of Dr. Winston Turner, a daughter.

DEATHS

Acomb.—On January 21, 1955, in South Africa, John Acomb, M.B., B.S., D.L.O., of Linton, late of York, Yorks.

Allen.—On January 19, 1955, at Allendale, Coonoor, South India, Charles Harry Powell Allen, M.R.C.S., L.R.C.P., Lieutenant-Colonel, I.M.S., retired.

Aung.—On January 18, 1955, at Edinburgh, Shway Hla Aung, M.B., B.S., of Rangoon, Burma, aged 33.

Bell.—On January 29, 1955, at the Manor House, Buckden, Huntingdon, Arthur Sydney Gordon Bell, M.R.C.S., L.R.C.P., Surgeon Commander, R.N., retired.

Boone.—On January 27, 1955, at Hove, Sussex, William Brooke Boone, B.M., B.Ch., of Hillsborough Terrace, Ilfracombe, Devon.

Browne.—On January 29, 1955, at the Long House, Little Strickland, near Penrith, Westmorland, Peter Otho Watkin Brown, M.B., C.M., late of Alderley Edge and Nethy Bridge, Inverness-shire, aged 88.

Burns.—On January 20, 1955, Henry Burns, O.B.E., M.B., Ch.B., Surgeon Commander, R.N., retired.

Butterworth.—On January 21, 1955, at Borth, Cardiganshire, John Butterworth, M.R.C.S., L.R.C.P., J.P., formerly of Middleton, Lancs, aged 83.

Castell.—On January 1, 1955, at his home, Finchley, London, N., Samuel Percy Castell, M.B., aged 61.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Collapse due to Adrenaline in Dental Analgesic

Q.—*What is the most efficient dental local analgesic injection for a patient who is intolerant of adrenaline? The patient has twice had a serious collapse after these injections in the dentist's chair, but wants to avoid a general anaesthetic.*

A.—"Cobefrin," an isomer of adrenaline, can be used as an alternative to adrenaline and is said to produce less general disturbance than the latter. Alternatively procaine can be used by itself, or better still the newer local analgesic solution "xylotox," which contains lignocaine hydrochloride in Ringer's solution. This itself produces a vasoconstrictor action and hence eliminates the need for adrenaline.

Diagnosis and Treatment of Psychosomatic Disorders

Q.—*What are the positive points to look for in making a diagnosis of a psychosomatic disorder? I often see patients with vague complaints of pain, in whom every investigation is negative, and suspect that some of these pains are psychological in origin. Having made such a diagnosis, what should I do then? Often a patient reacts very violently to any suggestion that he should be seen by a psychiatrist.*

A.—The term psychosomatic is used in two ways : (1) To describe a disability dependent upon emotional factors (for example, anxiety) which are expressed either as a symptom without an objective organic lesion or as a physical disturbance (for example, peptic ulcer) whose existence may be verified by the usual methods. The emotional disturbance affects the soma through the autonomic system. (2) Of a disability, predominantly or wholly organic in origin, which leads to an emotional disturbance (for example, worry following the amputation of an arm).

An affirmative diagnosis of psychosomatic illness requires a careful history of the present illness, and in particular an atmosphere of emotion at the onset of the illness should be looked for. The emotion may be prolonged and figure largely in the clinical picture. The patient's description of the illness is generally overcoloured. Often, too, there will be a collection of medical reports with inconclusive diagnoses. A note should also be taken of the patient's reaction to past events such as the demands of school, work, marriage, and previous ill-health. Soon a picture of his personality will emerge. Happy and harmonious people do not develop psychosomatic complaints. The practitioner therefore should ask himself, What made this person ill ? The answer will involve an assessment of the relative importance of those constitutional, environmental, and personal elements which predisposed the patient to develop the signs and symptoms he now has.

Vague complaints of pain, if persistent and without organic change, suggest a diagnosis of conversion hysteria or of an anxiety state. Presumably "every investigation" does not include a psychological investigation. Exhaustive physical examinations alone may induce an iatrogenic neurosis.

In treatment, a wise course is to affirm the reality of the illness, to state its nature as partly physical and partly emotional, and to explain that it is not due to "imagination" or "lack of will-power." Further, that for advice on treatment the help of a specialist—that is, a psychiatrist—would be desirable. Should the patient find this suggestion distasteful the physician should express regret and, without argument, he should recommend the patient to think it over. If the patient, after reflection, still refuses the consultation it should be assumed that he has some misconceptions about psychiatrists or some shyness about the questions he fancies he might be asked. Both topics should be discussed frankly.

Treatment of Hodgkin's Disease

Q.—*Would you kindly tell me if anything is known in this country about the treatment of Hodgkin's disease by a mould, actinomycin C ? This substance is used, I believe, in Germany. What do you consider the best treatment for this disease ?*

A.—Actinomycin C, which is related to actinomycin A, was tried as a chemotherapeutic agent against human malignant disease in Germany. According to Schulte,[1] the substance was inactive in carcinoma and in leukaemia, but had a temporarily beneficial effect in Hodgkin's disease. Most of the cases treated had concurrent radiotherapy ; however, a few who were treated exclusively with actinomycin C showed a temporary reduction in the size of superficial tumours. Mediastinal masses, however, were unaffected. Recently a number of trials of actinomycin C ("sanamycin") have been made in France. The results of these trials[2] showed a very limited response in a very small proportion of the cases of Hodgkin's disease. Its side-effects included stomatitis and diarrhoea.

In the author's opinion the published results with actinomycin C are inferior to those obtained with nitrogen mustard or T.E.M. (triethylene melamine). Both nitrogen mustard and T.E.M. will produce a remission of several months in most cases. Actinomycin C is said not to affect the veins on injection, as occurs with nitrogen mustard. This advantage can also be claimed for T.E.M., which is an oral preparation. The depressant effect on bone marrow is apparently less with actinomycin ; this would be an advantage over both nitrogen mustard and T.E.M. if the clinical effectiveness of actinomycin was as great. This does not seem to be the case.

None of the chemotherapeutic agents so far described can yet replace radiotherapy in the treatment of the early or moderately early case of Hodgkin's disease. When radiotherapy can no longer be employed, or in the late generalized case, chemotherapy with nitrogen mustard or T.E.M. is valuable in affording one or more remissions of the disease. In the still later stages a further remission can be obtained in some cases with A.C.T.H. or cortisone.

REFERENCES

[1] Schulte, G. (1952). *Z. Krebsforsch.*, **58**, 500.
[2] *Presse méd.*, 1954, **62**, 737.

Distended Bladder in a Child

Q.—*When examining the abdomen of a boy aged 4 years 7 months who was suffering from diarrhoea and vomiting, I found his bladder distended almost to the umbilicus. With small encouragement he passed a pint (570 ml.) of urine without discomfort. He has no phimosis, pin-hole meatus, or obvious cause for retention of urine. His distended bladder seemed to cause him no discomfort. Are such cases unusual ? Do they require watching or active treatment ?*

A.—A bladder as full as this is found now and then in the course of examining children, and is of no consequence provided that, as in this case, the child is able to pass urine normally. It probably results simply from the dislike of some children of asking to go to the lavatory, or if in bed of asking for the pot, until the very last minute. No treatment is indicated.

A distended bladder may occur in chronic constipation of severe degree, but the latter is then obvious on account of the faecal lumps in the loaded colon. Bladder neck obstruction or a urethral valve will cause chronic distension of the bladder. In this case, if micturition is watched the stream is seen to be feeble and intermittent, and the bladder is not usually fully emptied.

Prolapse in Young Women

Q.—*Is it worth carrying out an operative repair in young women with prolapse, or does the likelihood of further pregnancies make this a waste of time?*

A.—Youth and the possibility of further childbearing do not contraindicate operative treatment for prolapse, but they may call for modifications in surgical technique. In particular, every effort should be made to avoid amputating the cervix at the time of colporrhaphy, for this may lower fertility, cause abortion, or complicate labour. Indeed, every delivery following amputation of the cervix should be carried out in hospital.

If the operation is restricted to afterior and posterior colporrhaphy, subsequent pregnancies are not likely to be complicated and the risk of a recurrence of prolapse is not very high. It is usually advisable, however, to carry out episiotomy in labour. Even if the prolapse should recur after further childbearing and require another operation, the original operation is not to be regarded as a waste of time. It is unreasonable to condemn women to endure a prolapse for many of what should be their most active years, their only consolation being that they will be made comfortable when they reach an age at which the comfort means less to them.

*** This answer is taken from the third book of *Any Questions?* Copies of the second and third books of *Any Questions?*, each containing some 200 expert answers, are available from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller, price 7s. 6d. a copy (postage 6d.). The third book contains a cumulative index.

Sea Travel for the Elderly

Q.—*Are there any special contraindications to elderly people undertaking long voyages by liner? Are any special precautions advised?*

A.—There are no special contraindications to elderly people undertaking long sea voyages provided they are in average good health.

If the voyage involves passage through tropical waters it is desirable that they should travel at a cool period of the year. May and September are both trying months in the Red Sea, and in the period June to September when the S.W. monsoon is blowing conditions are hot and humid in the Indian Ocean. Apart from this the individual should be instructed to carry out on board so far as is practicable the normal routine he has been accustomed to in his own home, from the point of view of both exercise and diet. When the weather is hot he will be well advised to cut down exercise, perhaps spend one or two days resting in bed during the hottest period of the voyage, and throughout the hot-weather period he should drink water freely and add a little salt to this water.

The passenger should be reassured by the knowledge that in case of need there is on board a competent medical staff.

Is Chlorbutol a Dangerous Preservative?

Q.—*Chlorbutol is used as a preservative for some types of injection. Have any untoward effects been ascribed to it when used in this way?*

A.—Chlorbutol has been used for nearly 50 years as a preservative for solutions of adrenaline and of posterior lobe extract for hypodermic injection, being present in a strength of 0.5%, and has not produced untoward effects. The preservative. The Council of Pharmacy and Chemistry of the American Medical Association[1] recommends it as the best preservative for ophthalmic solutions, as it is non-toxic, non-irritant, and free from a tendency to produce sensitization. Chlorbutol can be used orally as a sedative and antispasmodic, for which purpose the dose is 0.3–1.2 g. general view about chlorbutol is that it is a safe and useful It was the main constituent of Mothersills' remedy for sea-sickness. Toxicity does not arise with amounts less than 6 g. (90 gr.) by mouth.

REFERENCE

[1] *J. Amer. med. Ass.*, 1953, **152**, 1631.

A Damp Cottage

Q.—*A patient is worried because she has gone to live in an old cottage which in summer was dry but now shows a lot of damp patches on the walls of the ground-floor rooms. Is she running any real health risk, and, if so, of what?*

A.—Tradition is in favour of this patient's fears. Science, however, has never demonstrated any direct deleterious result on a person in normal health living in a damp house. The fact that it is damp implies that the temperature inside tends to be less than that outside, owing to evaporation from the walls. The effect on the occupants will be to contract the skin capillaries, which some authorities consider may depress general immunity processes in some people, and in rheumatic subjects often to increase the pain suffered. But this can usually be counteracted by the installation of an adequate heating system.

Chickenpox, Zoster, and Poliomyelitis

Q.—*Is there any evidence to suggest that an attack of chicken-pox or herpes zoster protects against poliomyelitis?*

A.—No information is available on the question of whether previous exposure to varicella or zoster protects against poliomyelitis. It would seem unlikely on general grounds that such a widespread infection as chickenpox could protect against poliomyelitis without being noticed. It is certain that circulating antibody from previous infection with varicella-zoster virus is unlikely to have any protection against poliomyelitis, as the two viruses are antigenically unrelated.

NOTES AND COMMENTS

Fetishism.—OUR EXPERT writes: In your issue of January 29 (p. 302) Dr. Doris Odlum comments on my reply to a question on this subject ("Any Questions?" January 15, p. 178). The female patients whom Dr. Odlum considered to be suffering from fetishism were free from any kind of emotional disturbance and all were making a good adjustment to life. She adds that the condition—that is, fetishism—was not due to any morbid tendency but represented "an alternative or supplementary form of sexual gratification." She implies that any object which excites erotic feelings is a fetish. But this is not the sense in which the term is used in psychiatric literature. The true fetishist finds that coitus is impossible without the fetish object or the phantasy of it. There is no question of having the fetish as "an alternative or supplementary form of sexual gratification."

Dr. Odlum implies that fetishism is common among women, but unrecognized because they do not talk of such socially unacceptable matters. This is not very convincing, for male fetishists have exactly the same reluctance and even during psychotherapy there is hesitation in mentioning the subject. One or two examples of fetishism in women have been reported in psychoanalytical literature; yet few psychoanalysts have been dogmatic about the existence of fetishism in females. Other workers with wide experience say that they have never come across an example or that it is extremely rare. The writer has made considerable inquiry in the past from psychiatrists of different schools of thought and so far has been unable to find a single authenticated instance of fetishism in women. Hence the statement that fetishism does not seem to occur in women.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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